CARDIAC DIAGNOSIS

A Physiologic Approach

BY

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Preface

This book represents an approach to cardiac diagnosis based on the function and control of the heart under normal and abnormal conditions emphasizing the mechanisms by which disease processes produce various signs and symptoms Since these mechanisms are described in terms of physical and physiologic principles as applied to clinical problems the text is intended for students of medicine in the broadest sense from first year medical students to experienced physicians who are interested in applying basic concepts to the recognition of disease processes Thus the organization and content were designed as a vertical presentation of cardiovascular physiology and cardiac diagnosis Such a book seems timely because of recent revolutionary changes in the status and philosophy of cardiology Many of the traditional concepts of cardiac function and control have been questioned or modified in recent years Rapid advances in both prophylaxis against rheumatic fever and surgical therapy of many types of valvular and congenital heart disease greatly increase the need for accurate diagnosis At the same time developments in cardiac surgery have provided an opportunity for checking the clinical diagnosis directly in the living heart The observations made during surgery have given very little basis for complacency regarding the accuracy of clinical diagnosis because errors have been embarrassingly frequent For example it is becoming clear that the location nature and severity of valvular lesions cannot be consistently determined from heart murmurs The need for more accurate preoperative diagnosis calls for more quantitative measurements of the significant variables Cardiac catheterization is an example of the growing emphasis on the *science* of medicine as a supplement to the *art* of medicine Other technologic advances in this category are methods for estimating cardiac output devices for measuring pressure and specialized roentgenographic procedures such as angiocardiography and electrokymography

Although every physician acquires knowledge of basic physiologic principles clinical diagnosis is still too largely dependent upon correlations of specific disease processes with characteristic patterns of signs and symptoms Thus clinical teaching and textbooks depend mainly on descriptions of individual disease entities The *descriptive* approach gives the impression that diagnosis is relatively simple However a substantial proportion of patients exhibit quite different responses to the same disease processes so the different combinations of signs and symptoms are unlimited The characteristic signs and symptoms are fully developed only after a disease process is well advanced and are often equivocal during early stages when diagnosis is most important Finally diagnosis based on subtle and empirical signs often obscures the functional similarity between widely different disease processes In this particular physiologic approach to cardiac diagnosis analyzing the functional effects of various disease processes emphasizes the points of similarity as well as the differences between various types of heart disease

The organization of the book is simple Since the heart must be considered in its relation to the entire circulatory system the first four chapters (Part I) are devoted to the

anatomic, physical and functional aspects of the whole cardiovascular system Part II consists of three chapters on the regulation of the peripheral vascular system and of the heart, reflecting the growing emphasis on neural and hormonal control In Part III, congestive heart failure is analyzed using a comprehensive schema of the factors in cardiac reserve and their interrelationships Part IV presents both old and new diagnostic techniques, including their basic principles, methods of procedure, usefulness and limitations The application of all these fundamental concepts and diagnostic methods to clinical problems encountered among five main categories of heart disease constitutes Part V These discussions are intended to indicate how physiologic principles apply to the diagnosis of selected conditions rather than to provide a complete dissertation on heart disease

The illustrations are distinctive in respect to both their nature and their utilization Important ideas in each chapter have been illustrated in order to facilitate discussion and aid visualization of concepts The figures are intended to explain ideas rather than offer evidence for arguments Realism in the schematic drawings has been retained as much as possible to provide visual images of physiologic and pathologic mechanisms in situ rather than as abstractions The legends for each figure are self explanatory and render the illustrations independent of the text Cross references are made to figures rather than text pages in the belief that it is more efficient to refresh the memory through pictures than by rereading the text

Graphs and tables have been avoided for two reasons (*a*) their interpretation is often difficult and tedious and (*b*) it seems more important to understand *why* certain phenomena occur rather than *how much* specific variables are altered under experimental conditions Graphs tend to suggest cause-and-effect relations which do not exist When experimental records are reproduced a schematic representation of the experimental method is also included

References have been cited to defend a position or to provide sources of additional information which I feel may interest the reader By definition, the references cited in classic contributions are likely to be outmoded For this reason, priority has been given to recent publications because they provide a much more convenient point of departure for further reading This decision unfortunately results in failure to ascribe due credit to many investigators who have contributed to our fund of knowledge

At the risk of appearing excessively biased, I have tried to avoid exhaustive presentations of conflicting viewpoints If a single hypothesis appeared adequate to explain a particular phenomenon, alternative explanations have not necessarily been included Attention has been directed to many deficiencies in current knowledge which can be corrected only by further investigations

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Acknowledgements

A book of this sort represents a small sample of facts and concepts selectively extracted from a vast store of material on the subject. The final content of this manuscript has been influenced by a series of research projects accomplished in association with a closely knit research team representing several fields of interest including Messrs Richard M Ellis electronics engineer John A Hendron Jr and Alden A Nash x ray technicians Dean Franklin electronics technician and Drs Dean K Crystal Clyde Wagner Allan W Lobb and Bliss L Finlayson surgeons The ingenuity persistence and technical competence of this group were indispensable to the successful completion of the studies some of which are summarized in this text The various research projects were supported in part by grants from the National Heart Institute of the National Institutes of Health United States Public Health Service the Washington State Heart Association and the American Heart Association and the Washington State Fund for Biology and Medicine

I am indebted to a number of colleagues for reviewing and criticizing certain portions of the manuscript including Drs T C Ruch Allan C Young H D Patton Richard Blandau and Russell Weiser My close association with Dr Robert A Tidwell and other members of the Cardiac Clinics and staff of the Children s Orthopedic Hospital has been invaluable Dr Allen M Scher summarized his recent investigations in Chapter 15 Miss Lois Swanson carried the heavy secretarial load and I gratefully acknowledge her interest cooperation and patience in the preparation of the manuscript Mrs Maryeva Terry contributed greatly through her expert editorial revisions and suggestions concerning the planning of the format I gratefully acknowledge the wholehearted cooperation of the W B Saunders Company in the production of the book

Most of the illustrations were designed and executed by the author although many were refined and labeled by Miss Jessie Phillips Mrs Helen Halsey Miss Virginia Brooks and Mrs Mary Jane Owens The relatively small number of signed drawings is no indication of their contribution to the illustrations in the book Half tone drawings of congenital malformations of the heart in Chapter 19 were executed by Miss Phillips for a series of three motion picture films directed by the author produced by Mr Ralph Pearson and sponsored by Dr and Mrs Maimon Samuels (see reference 1, Chapter 19) Photographic reproductions were prepared by Mr John Newby and Mr Roy Hayashi

Several of the original illustrations in this book first appeared in articles by the author and his associates in the following journals *American Heart Journal* (Figs 13 and 14 Chapter 13 Figs 5 12 and 13 Chapter 17) *American Journal of Physiology* (Fig 9 Chapter 3 Fig 4 Chapter 6) *Circulation* (Figs 8 9 and 13 Chapter 1) *Circulation Research* (Fig 3 Chapter 1 Figs 5 and 6 Chapter 6 Fig 7 Chapter 7 Figs 10 4 and 12 Chapter 15) *Journal of Pediatrics* (Fig 20 Chapter 19) *Minnesota Medicine* (Fig 11 Chapter 7) and *Physiological Reviews* (Figs 9 and 14, Chapter 6) I wish to express my appreciation to the publishers of these journals for permission to reproduce the illustrations

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FUNCTION OF THE NORMAL CARDIOVASCULAR SYSTEM

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Functional Anatomy of Cardiac Contraction

A physician is best prepared to assume the responsibility for preventing, detecting and treating organic disease of the heart when he understands the basic mechanisms of cardiac function as clearly as possible in the light of current knowledge. The two fundamental requirements of the cardiovascular system are (*a*) circulation of blood without interruption and (*b*) regulation of blood flow in response to the varying demands of the tissues. If the circulation is interrupted even briefly, survival of the individual is jeopardized. If a patient loses the normal ability to increase the volume flow of blood in response to demand, he is restricted in the amount of physical activity and useful work he can perform. Extreme limitations in the ability to increase cardiac output produce bedridden patients. Fundamentally, the heart must continuously adapt its output to balance the flow through the billions of capillaries in the body. Cardiac output is normally increased by tachycardia and by augmented stroke volume. If the ability to augment stroke volume is impaired by disease, the energy released by the heart as a pump is seriously reduced.

The energy released during ventricular systole represents the combined efforts of the various bundles of myocardial fibers. The contribution of each bundle depends not only on its contractile power but also on its anatomic orientation within the cardiac walls. This chapter is devoted to describing the functional anatomy of cardiac contraction as a background which is essential for an understanding of cardiac adaptability and control.

ANATOMIC COMPONENTS OF THE HEART

Four rings of dense connective tissue are joined to form a single fibrous skeleton of the heart. The atria, ventricles, valves and arterial trunks are all firmly attached to this skeleton (Fig. 1). The two atria resemble a thin walled, shallow cup of myocardium divided by a partition down the center. Each atrium has an atrial appendage, the functional significance of which is completely unknown. The margins of the atrial shell are fastened to the superior surface of the mitral and tricuspid valve rings.

The aorta and the pulmonary arteries originate at the superior surface of the corresponding semilunar valve rings. Thus the atrial chambers and the arterial trunks are anchored to the superior surface of the fibrous skeleton. The inflow and outflow channels of each ventricle lie side by side. The atrioventricular (A-V) valves are fastened to the inferior surface of the mitral and tricuspid valve rings with the fibrous connective tissue at the root of each valve leaflet merging with that of the corresponding valvular ring. Chordae tendineae extending from the inferior margins of each leaflet of the A-V valves are fastened directly to the internal surface of the ventricular walls and to papillary muscles projecting from the endocardial surface of the ventricular chambers.

The right and left ventricles are fastened to the entire circumference of the fibrous skeleton of the heart. The upper margin of the interventricular septum is attached along the line of fusion between the mitral and

Introduction to Part One

Since the heart is an integral portion of the circulatory system, disease of the heart frequently produces abnormal function in the peripheral circulation while pathologic changes in the vascular systems often affect the heart For this reason, the functional anatomy of each component of the cardiovascular system will be considered in the first four chapters to view the heart in its proper perspective The heart functions as a pump by actively changing the dimensions of the individual chambers Thus, an accurate visualization of cardiac function requires information concerning both the anatomic components and their contribution to the total contraction process For this reason, Chapter 1 deals with the anatomic, geometric architectural and functional characteristics of cardiac contraction

The work load of the individual ventricular chambers is actually dictated by conditions in the circulatory bed into which it ejects blood The functional anatomy and physical characteristics of the systemic circulation directly affect the operational conditions of the left ventricle, as indicated in Chapter 2 Since much of man's existence is spent in the erect position, Chapter 3 is devoted to the circulatory adjustments required to sustain the pressure and flow of blood when a normal individual stands or walks The structural functional and physical properties of the pulmonary vascular bed are considered in a separate chapter (Chapter 4) to emphasize the differences between the pulmonary and systemic circuits

cardial fibers primarily oriented in three general directions The inner and outer layers are spiral muscles which follow oblique courses approximately 90 degrees apart since they spiral in opposite directions As the spiral muscle bundles contract the oblique traction by the outer layer is counteracted by tension developed in the opposite direction by the inner layer The combined effect of their contraction is a shortening of the chambers along their longitudinal axes rather than a rotation of the ventricles Because of the swirling intertwining and overlapping of the superficial bundles along their course down toward the apex and back toward the base the spiral layers are thin near the base and thick near the apex where they constitute the full thickness of the wall

The deep myocardial bundles lying between the external and internal spiral layers encircle the basilar two-thirds of the ventricular chambers These layers have been labeled the constrictor muscle because their shortening acts to reduce the diameter of the chambers like the clenching of a fist The left ventricle and the interventricular septum contain a large mass of deep constrictor fibers while the right ventricle contains a relatively thin layer of these fibers

Because of the large mass of constrictor fibers in the left ventricular wall its contraction produces primarily a reduction in the chamber s diameter with a smaller degree of

ANATOMY OF THE VENTRICULAR WALLS

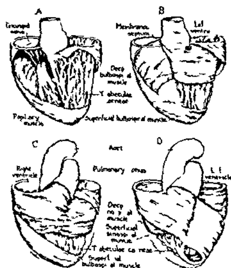


FIGURE 2 *A* The superficial bulbospiral muscle bundles arise principally from the mitral ring and form the external investment for portions of the left and right ventricles as they spiral toward the apex Emerging from the vortex on the inside of the chambers these muscle bundles spiral back toward the valve rings either as trabeculae carneae or as papillary muscles which are joined to the valves through chordae tendineae

B The deep bulbospiral muscle fibers encircle the basilar portions of the left ventricle

C The deep sinospiral muscle encircles both the right and the left ventricular chambers

D The superficial sinospiral muscle is a counterpart of the superficial bulbospiral muscle The anatomic distinction between the superficial sinospiral and bulbospiral muscles is arbitrary and functionally unimportant (After Robb and Robb [3])

FUNCTIONAL COMPONENTS OF VENTRICULAR MUSCULATURE





FIGURE 3 The muscular architecture of the ventricles is illustrated by schematic drawings

A Blocks of tissue removed from the walls of the ventricles are composed of three layers of muscle The myocardial fibers in these layers are oriented roughly in the three general directions indicated by the arrows

B From a functional point of view the ventricles are formed of two sets of myocardial bundles (*a*) the internal and external layers of spiral muscle which enclose (*b*) the ventricular constrictor muscles The internal and external investments of the ventricular chambers are composed of the same muscle bundles which are strongly twisted at the vortex and spiral in opposite directions from the apex toward the base

ANATOMIC COMPONENTS OF THE HEART

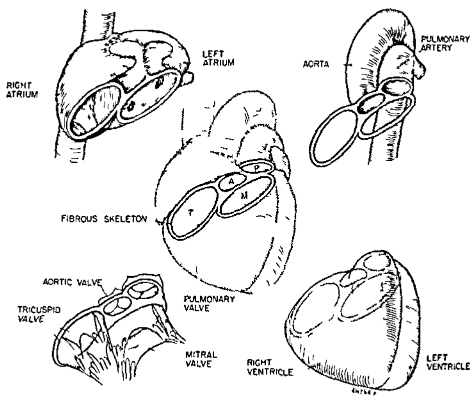


FIGURE 1 The fibrous skeleton of the heart consists of four valve rings joined together To these dense connective tissue annuli fibrosi are fastened the two major arterial trunks and all four cardiac chambers The atria and arterial trunks are attached to the superior surface of this fibrous skeleton and the ventricles and atrioventricular valve leaflets are fastened to its inferior aspect

tricuspid valve rings The membranous portion of the septum is fused at the junction of the pulmonary and aortic valve rings

The Anatomy of the Ventricular Walls

The ventricles serve as the major source of energy for the circulation of blood and are composed of sheets of myocardial fibers encircling the ventricular chambers in a complex fashion[1-3] reminiscent of the windings of a turban The various muscular layers in the ventricles are so tightly bound together that they are very difficult to dissect into individual components According to Robb and Robb,[3] the ventricular walls are composed of four different muscles the superficial sinospiral and bulbospiral muscles and the deep sinospiral and bulbospiral muscles (Fig 2) The superficial layers originate from the fibrous skeleton of the heart, spiral down toward the apex, enter the vortex and then spiral in the opposite direction back to their insertion on the fibrous skeleton The deep sinospiral and bulbospiral muscles also originate at the connective tissue of the valve rings and descend varying distances toward the apex They then encircle the ventricular chambers before ascending to their insertions on the fibrous skeleton Whether a muscle bundle is called "sinospiral" or "bulbospiral" depends solely upon the valve ring at which it originates This division is purely arbitrary and appears to complicate the picture unnecessarily

Functional Components of *Ventricular Musculature*

From a functional point of view, the ventricular musculature can be divided into two groups of myocardial bundles,[4] the spiral muscles and the deep constrictor muscles as illustrated schematically in Figure 3 A block of tissue cut from the mid portion of the right or left ventricular wall contains myo-

terminate in the immediate vicinity[4] and discharge of the vagal fibers releases acetylcholine which tends to slow the rate of impulse formation. The sympathetic fibers release epinephrine-like substances which act to accelerate the frequency of impulse formation.[6] Since the vagal influence generally predominates, the "normal" heart rate ranges between 60 and 100 impulses per minute. The S-A node retains its position as pacemaker for the entire heart so long as it generates impulses at a faster rate than any other region of the myocardial syncytium and so long as the spreading wave of excitation is rapidly conducted from the atria to the ventricles.

The Sequence of Excitation

There is no apparent conduction system in the atria so a wave of excitation originating in the S-A node spreads out in all directions like the concentric wave produced by dropping a pebble into a pool of water. It travels at a rate of about 1 meter per second and reaches the most distant portions of the atrium in about 0.08 second. As it approaches the interatrial septum the wave of excitation reaches another mass of specialized conducting tissue, the atrioventricular (A-V) node.

The A-V node is located near the posterior margin of the interatrial septum close to the entrance of the coronary sinus (Fig. 5). When the wave of excitation reaches the A-V node it does not proceed directly to the ventricles but is delayed there for intervals ranging atmund 0.08 to 0.12 second. It has been suggested that this delay is due to slow conduction along delicate fibers connecting the atrial myocardium with A-V nodal tissue. During the A-V nodal delay, atrial contraction is largely completed. The A-V node is the bulbous end of a bundle of Purkinje fibers—the bundle of His—which passes forward along the right side of the interatrial septum before plunging downward across the A-V junction to the upper margin of the muscular interventricular septum. There it divides into two branches—the right and left bundles—which descend on opposite sides of the interventricular septum. The bundle branches ramify into a network of Purkinje fibers which is distributed over the inner surface of the ventricular chambers.

After leaving the A-V node, the wave of excitation passes rapidly (4 to 5 meters per second) along the Purkinje fibers of the common bundle and the bundle branches.[5, 7, 8] The exact course by which the wave of excitation is distributed throughout the ventricular musculature is not definitely established, but there is impressive evidence that the endocardial surfaces of the ventricular chambers are excited early (see Chapter 15). Thus the wave of excitation probably penetrates the ventricular walls from the endocardial to the epicardial surface. The rapid spread of excitation through the ven-

SEQUENCE OF CARDIAC EXCITATION

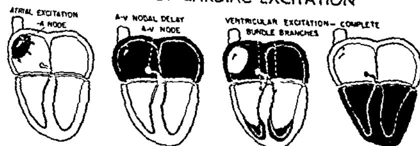


FIGURE 5. Excitation of the heart is normally initiated by an impulse which is generated by the S-A node and which spreads rapidly in all directions through the atrial musculature. After a slight delay at the A-V node, impulses are conducted by the Purkinje system into the ventricles where a wave of excitation spreads from the endocardial surfaces through the ventricular musculature.

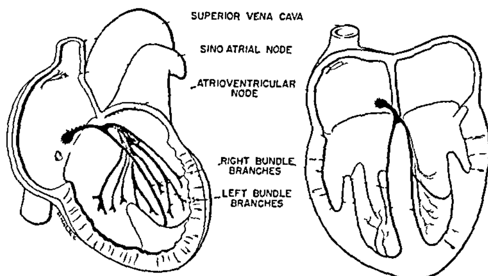


FIGURE 4 The sino-atrial node is the normal pacemaker of the heart No specialized conduction system has been described in the atria The A V node common bundle and bundle branches conduct the wave of excitation from the atrium to the ventricular myocardium

shortening along the longitudinal axis In the right ventricular wall, on the other hand the predominance of spiral muscle effects a large degree of ventricular shortening with relatively little movement of the free wall toward the septum Such shortening of the right ventricular chamber should tend to draw the tricuspid valve ring toward the apex of the heart These predictions have been confirmed by cinefluorographic studies of ventricular contraction (see Fig 11 and reference 4)

COORDINATION OF THE HEART BEAT

To produce efficient pumping the complex mass of myocardial bundles must contract more or less simultaneously The effectiveness of the ventricles is lost if the individual myocardial bundles contract in a random fashion, e g , in ventricular fibrillation Coordinated contraction of the complex pattern of myocardial bundles stems from the syncytial arrangement of the myocardial fibers excitation beginning at one site spreads to all other contiguous areas Excitation of the thick ventricular walls is facilitated by a rapidly conducting system of Purkinje fibers The conduction system is responsible for periodic initiation of excitation (pacemaker activity) a delay between atrial and ventricular contraction (A-V nodal delay) and the rapid spread of excitation to all portions of the ventricular walls so that their contraction is sufficiently simultaneous to produce effective pumping action When the conduction system is operating normally, this stereotyped sequence of events is repeated during each successive cardiac cycle

The Conduction System of the Heart

The sino-atrial (S-A) node is a small mass of specialized myocardial tissues embedded in the atrial wall near the entrance of the superior vena cava (Fig 4) This node consists of an accumulation of modified myocardial cells Shaped like an Indian war club, it has a fringe of delicate fibers merging with surrounding myocardial fibers The S-A node is the normal pacemaker spontaneously originating the spreading waves of excitation at a more rapid rate than any other part of the heart (see Chapter 14) If it were isolated from all neural and hormonal control the S-A node would probably generate impulses at a rate in excess of 100 per minute However, a large number of fibers from the parasympathetic and sympathetic nervous systems

physiologic events, e g timing of heart murmurs and analysis of electrocardiograms or arterial and venous pulse contours

The energy released by cardiac contraction is expended primarily in elevation of the blood pressure within the ventricular cavities and in impelling the blood from the ventricles into the arterial trunks Since myocardial contraction produces changes in the pressure and volume of blood in the ventricles the sequence of events can be conveniently described in terms of the atrial ventricular and arterial pressures and of the variations in the combined volume of both ventricles as measured by a cardiometer (Fig 7)

The Mechanical Effects of Cardiac Contraction

During the later portion of diastole the ventricular pressure equals the atrial pressure because the two chambers are connected through the wide A-V orifices and little or no blood is flowing between them The wave of excitation spreading over the atrium is followed by atrial contraction The contraction slightly increases both intra atrial and intraventricular pressures because it suddenly compresses this portion of the venous volume reservoir As the atrium contracts blood may be displaced into the ventricular chambers or back into the large venous channels depending upon which course offers the least resistance The quantity of blood which enters the ventricle in response to atrial contraction is quite variable Excitation of the ventricles begins as atrial contraction is being completed and ventricular contraction begins about 0 07 second later [8] Ventricular pressure rises to exceed arterial pressure during the period of isometric contrac-

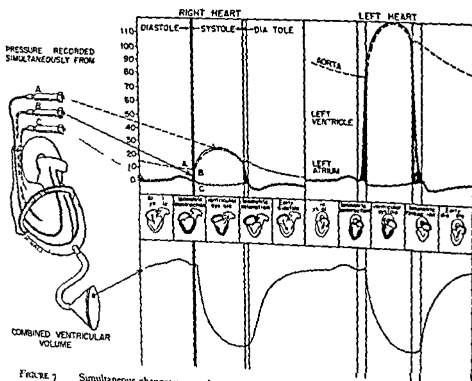


FIGURE 7 Simultaneous changes in atrial ventricular and arterial pressures in the right and left ventricles are illustrated schematically along with fluctuations in combined ventricular volume to indicate the sequence of events during a single cardiac cycle (see text) The great difference in pressure developed by the two ventricles is consistent with the differences in their architecture (see Fig 12)

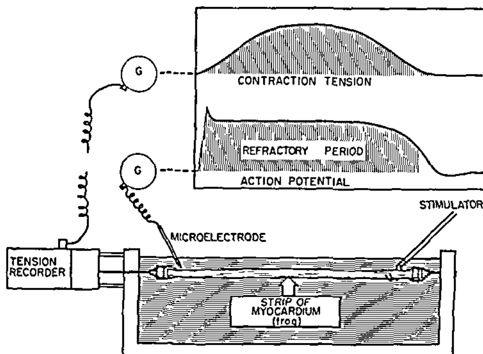


FIGURE 6 Simultaneous records of the electrical activity and contractile tension of a strip of myocardium demonstrate that the action potential persists during contraction Since the muscle fibers are refractory to stimulation while the membranes remain depolarized another contraction cycle is not normally initiated until after relaxation of the muscle and filling of the chambers have occurred (from Curtis H J Amer J Physiol 159 499–504 1949)

tricles produces more or less simultaneous contraction of the ventricular musculature It is apparent that waves of excitation originating at abnormal sites or following devious pathways will interfere to some extent with the coordinated contraction of the various chamber walls This problem will be considered in a subsequent section (Chapter 14) For the present, the discussion will be confined to normal cardiac cycles

Relaxation of the Heart

The pumping action of the heart requires alternate periods of contraction and relaxation Since the ventricles eject only the blood that enters the chambers during the interval between contractions relaxation of the myocardium is just as important as contraction A sustained contraction corresponding to tetanus in skeletal muscle would completely eliminate effective pumping by the heart Summation of contractions and tetanus in myocardium never occurs under normal conditions because the heart muscle remains refractory to stimulation during a major portion of its contraction This important attribute of myocardium stems from the fact that the excitatory 'membranes of the myocardial fibers remain depolarized during the period of contraction (Fig 6) A more detailed comparison of myocardium with other forms of muscle appears in a subsequent section (see Fig 2 Chapter 7)

THE SEQUENCE OF EVENTS DURING THE CARDIAC CYCLE

So long as the heart receives excitation along the normal pathways and the heart rate remains constant each successive cardiac cycle tends to follow the same pattern of contraction and relaxation A clear picture of the mechanical events of the cardiac cycle is required for logical interpretation of many

physiologic events e.g., timing of heart murmurs and analysis of electrocardiograms or arterial and venous pulse contours

The energy released by cardiac contraction is expended primarily in elevation of the blood pressure within the ventricular cavities and in impelling the blood from the ventricles into the arterial trunks. Since myocardial contraction produces changes in the pressure and volume of blood in the ventricles, the sequence of events can be conveniently described in terms of the atrial, ventricular and arterial pressures and of the variations in the combined volume of both ventricles as measured by a cardiometer (Fig. 7).

The Mechanical Effects of Cardiac Contraction

During the later portion of diastole the ventricular pressure equals the atrial pressure because the two chambers are connected through the wide A-V orifices and little or no blood is flowing between them. The wave of excitation spreading over the atrium is followed by atrial contraction. The contraction slightly increases both intra-atrial and intraventricular pressures because it suddenly compresses this portion of the venous volume reservoir. As the atrium contracts, blood may be displaced into the ventricular chambers or back into the large venous channels, depending upon which course offers the least resistance. The quantity of blood which enters the ventricle in response to atrial contraction is quite variable. Excitation of the ventricles begins as atrial contraction is being completed, and ventricular contraction begins about 0.07 second later.[8] Ventricular pressure rises to exceed arterial pressure during the period of isometric contrac-

MECHANICAL EFFECTS OF CARDIAC CONTRACTION

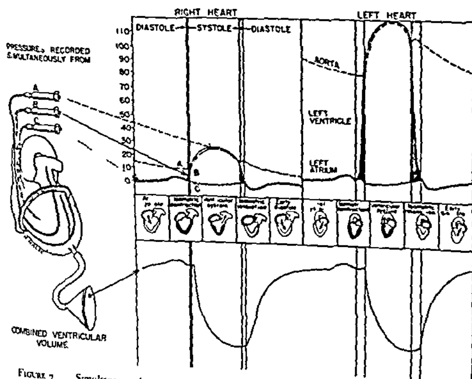


FIGURE 7 Simultaneous changes in atrial, ventricular and arterial pressures in the right and left ventricles are illustrated schematically along with fluctuations in combined ventricular volume to indicate the sequence of events during a single cardiac cycle (see text). The great difference in pressure developed by the two ventricles is consistent with the differences in their architecture (see Fig. 12).

tion, which lasts about 0 013 second in the right ventricle[9] and about 0 06 second in the left ventricle (Fig 7)

During this period the ventricular volume is unchanged except for the movement of blood required to close and displace the valves Thus, the period of isometric contraction is characterized by a slight reduction in recorded ventricular volume and a slight increase in atrial pressure due to ballooning of the A-V valves The atria relax and begin to refill during ventricular systole Isometric contraction of the ventricle ends when the ventricular pressure exceeds the arterial pressure and is followed by rapid ejection of blood into the arterial system Thus, the arterial pressure is elevated while the ventricular volume is abruptly diminished The intraventricular and arterial pressures tend to level off and descend as the rate of ejection from the ventricles drops below the rate at which blood leaves the arterial system through the capillaries The onset of ventricular relaxation is associated with a rapid drop in ventricular pressures below arterial pressure The semilunar valves become approximated by a retrograde surge of blood in the root of the aorta which produces the dicrotic notch in the arterial pressure wave During the period of isometric relaxation *ventricular pressure rapidly descends to a* level below the atrial pressure The A-V valves swing open before a gush of blood from the atrium The ventricles rapidly refill *with blood from the thoracic veins and atria,* as indicated by the abrupt upswing in the ventricular volume curve The slope of the volume curve indicates that early filling of the ventricles is more rapid than the ejection of blood by ventricular contraction Ventricular filling is largely complete very soon after the onset of ventricular relaxation and, if the diastolic interval is sufficiently long, ventricular volume reaches a plateau during which no more blood enters from the atrium —the period of diastasis The length of the diastolic interval is determined largely by the time required for the pacemaker to discharge the new wave of excitation which initiates another cardiac cycle

The Cardiac Cycle as Observed by Cinefluorographic Angiocardiography

X-rays penetrating the body of a dog illuminate a fluorescent screen producing an image of the cardiac silhouette Motion pictures of these images record changes in the size and shape of the heart If a radiopaque substance such as Diodrast is rapidly injected into the jugular vein, the course of the *opacified blood can be followed through the*

ROENTGENOGRAPHIC ANATOMY OF DOG HEART

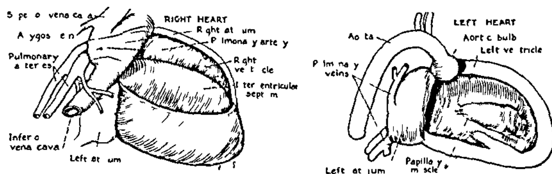


FIGURE 8 The anatomic relations of the cardiac chambers and arterial trunks are illustrated in the dog as viewed from the right side for comparison with angiocardiograms presented in subsequent figures The right atrium lies above the left atrium on the posterior aspect of the heart The interventricular septum presents a convex surface to the right ventricular cavity Thus the right ventricular cavity has a crescentic transverse section and partially encircles the left ventricular cavity

CHANGES IN SIZE AND SHAPE OF THE RIGHT ATRIUM AND VENTRICLE



FIGURE 9 Successive frames from a cinefluorographic film exposed at 15 frames per second illustrate the filling and contraction of the right atrium and right ventricle during 3.2 seconds following the injection of contrast medium. Examine each column in succession from above downward to observe the sequence of events

heart and great vessels[10] The changes in size and configuration of the individual cardiac chambers can be visualized as a two-dimensional projection or silhouette For purposes of orientation the anatomic relations of the great vessels and cardiac chambers in the heart of the dog are indicated in Figure 8 as viewed from the right side Note that the right ventricle does not extend to the apex of the heart in the dog Further, the configuration of the ventricular chambers is not the same in dogs and in humans Although the fundamental principles of cardiac contraction in dogs probably resemble those in humans, caution must be exercised in applying the discussion which follows to cardiac function in man

The typical sequence of events which occurs during filling and contraction of the right atrium and right ventricle of a dog is illustrated in Figure 9 Diodrast flowed along the superior vena cava during the eight frames in column *A* and entered the right atrium in the third frame of column *B* (*B*-3) In frame *B*-5, the tricuspid valves everted into the right atrium and blood gushed into the right ventricle in the next frame (*B*-6) The variations in density of the right ventricular shadow in frames *B*-7 and *B*-8 represent the mixing of the incoming blood with the residual blood remaining in the ventricle after the preceding systole The next contraction began in frames *C*-5 and *C*-6, as indicated by the protrusion of the right atrial appendage associated with atrial systole In frame *C*-6, the right ventricle began to contract and in the next three frames was reduced to a small triangular area with its base at the tricuspid valves Between frames *C*-8 and *D*-1 (1/15 second), the right ventricle was filled and apparently remained unchanged in size until the succeeding contriction (*D*-8) During the remainder of this cycle, Diodrast passed through the right atrium and flowed into the inferior vena cava down to the level of the diaphragm against the oncoming stream of blood The opacified blood in the inferior vena cava returned to the heart during the next filling period The right ventricle did not distend noticeably during the latter part of diastole even when there was sufficient pressure to force Diodrast against the stream of blood into the inferior vena cava The fact

FILLING OF THE RIGHT VENTRICLE

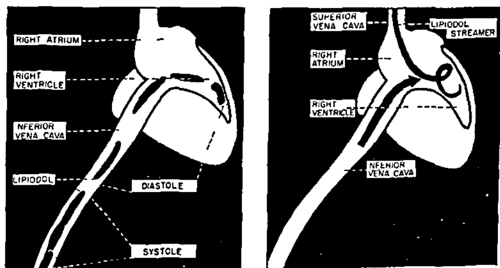


FIGURE 10 Lipiodol streamers floating freely in the blood move relatively slowly during one phase of the cardiac cycle then suddenly accelerate and move without hesitation into the right ventricular cavity presumably during the rapid filling phase of ventricular diastole (see text) Similar streamers of Lipiodol descending along the superior vena cava frequently display a *swirling motion* which may be due to the convergence of the two currents of blood flowing into the atrium

that diastolic filling appears to be largely complete very early in the diastolic interval is consistent with the curve of combined ventricular volume illustrated in Figure 7

Diastolic Filling of the Right Ventricle

Diastolic filling of the right ventricle can be studied by injecting Lipiodol into a systemic vein Lipiodol is a radiopaque viscous oil which is very cohesive and tends to flow along with the stream of blood as a long ribbon or as multiple globules depending upon how it is injected The course of one Lipiodol streamer ascending the inferior vena cava is indicated by serial tracings in Figure 10 The movement was relatively slow during systole At the beginning of the rapid filling in early diastole the Lipiodol streamer accelerated rapidly passing along the inferior vena cava through the atrium and into the right ventricle Thus the blood which fills the right ventricle comes not only from the atrium but also from a considerable distance down the inferior vena cava This description does not conform to the observations of Brecher[11] that the blood flow into the right atrium is most rapid during ventricular systole apparently owing to the aspirating effect of the shortening ventricular chamber The differences may be due to the fact that timing of events from these cinefluorographic films may not be sufficiently precise

Blood from the superior and inferior venae cavae converges at the right atrium Streamers of Lipiodol and Diodrast moving down the superior vena cava frequently exhibit a spiral flow as they enter the ventricle (Fig 10) This is attributed to a swirling motion of the blood produced by the confluence of the two streams These currents tend to mix the venous blood within the right ventricle

Contraction of the Right Ventricle

Cinefluorographic films indicate that a longitudinal section of the right ventricular chamber is roughly triangular in shape It is bounded by a convex septal wall and the concave free wall which enclose a crescent shaped slit between them (Figs 8 9) The action of the right ventricle resembles that of the old fashioned bellows used to kindle fires Since the sides of the bellows are large compared to the space between them their very slight movement toward each other causes displacement of a large volume from within In the right ventricular cavity a relatively narrow space is confined between two broad surfaces so that the surface area of the chamber is very great in relation to the volume 1- Additional details concerning the events in ventricular contraction have been

MOVEMENTS OF SPECIFIC POINTS ON THE VENTRICULAR WALLS

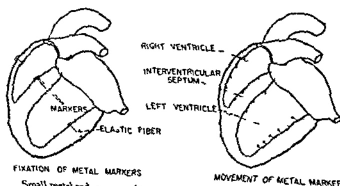
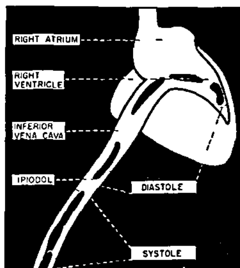


FIGURE 11 Small metal rods connected by resilient elastic fibers were mounted on opposite sides of the ventricular walls The positions of such markers on cinefluorographic films were noted during diastole and the general direction and magnitude of the movements of the endocardial surfaces during systole are indicated by the arrows on the right

heart and great vessels[10] The changes in size and configuration of the individual cardiac chambers can be visualized as a two-dimensional projection or silhouette For purposes of orientation the anatomic relations of the great vessels and cardiac chambers in the heart of the dog are indicated in Figure 8 as viewed from the right side Note that the right ventricle does not extend to the apex of the heart in the dog Further, the configuration of the ventricular chambers is not the same in dogs and in humans Although the fundamental principles of cardiac contraction in dogs probably resemble those in humans, caution must be exercised in applying the discussion which follows to cardiac function in man

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FILLING OF THE RIGHT VENTRICLE



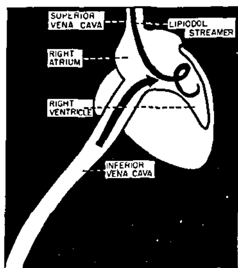


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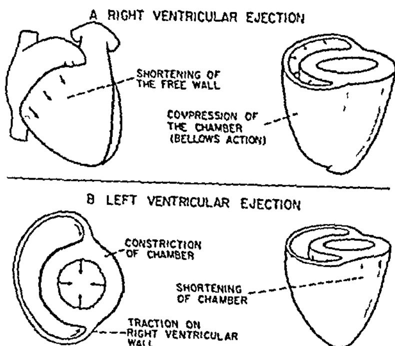


FIGURE 12. *A* Blood is ejected from the right ventricle by shortening of the free wall with downward displacement of the tricuspid valve ring and movement of the free wall toward the interventricular septum by myocardial shortening Compression of the right ventricular cavity may be supplemented by traction on the free wall by left ventricular contraction.
B Left ventricular ejection is accomplished primarily by a reduction in the diameter of the chamber with some additional shortening of the longitudinal axis

volumes of blood with minimal amounts of myocardial shortening On the other hand this architectural design is not conducive to the development of high intraventricular pressure [12] If the normal right ventricle were suddenly required to provide the intraventricular pressures normally developed in the left ventricle the right ventricular myocardium would have to develop tension many times as great as that of the left ventricle Thus we see that the right ventricle is specifically adapted to the task of pumping large or widely varying volumes of blood against a very low outflow pressure Since the pulmonary vascular tree normally offers slight resistance to flow the right ventricle normally ejects blood at relatively low pressure into the pulmonary artery (see Fig 7) However a sudden increase in pulmonary arterial pressure (massive pulmonary embolism) frequently leads to sudden death because the right ventricular myocardium is incapable of sustaining the higher pressures needed to provide adequate flow through the lungs If the pulmonary arterial pressure rises gradually, the right ventricle develops thick walls and a more cylindrical shape In other words the right ventricle adapts to a chronic pressure load by assuming some of the characteristics of the normal left ventricle

Left Ventricular Contraction

The left ventricular cavity resembles a cylinder with a conoid segment at the apical end (Figs 8 13) The cylindrical region is encircled by a strong cuff of deep fibers situated between thin layers of spiral muscle (see Fig 3) The conoid segment is made up primarily of the intricately intertwined spiral muscle bundles as they enter and leave the vortex Contraction of the left ventricle involves both a reduction in the diameter of the cylindrical portion and a shortening along

derived from cinefluorographic records showing metal markers installed on the internal and external surfaces of the ventricular walls Figure 11 summarizes the results of such experiments on ten dogs In this schematic diagram, movements of the markers during systole are indicated by the direction and length of arrows superimposed upon an outline of the ventricular chambers as they would appear during diastole Note that the general direction of movement of the right ventricular wall is *toward the apex of the right ventricle* The interventricular septum shortens very slightly along its longitudinal dimension but its central portion is not consistently displaced toward either the right or left ventricular cavities The free wall of the left ventricle tends to move simultaneously toward the interventricular septum and toward the apex of the heart Markers on the endocardial surface of the free ventricular walls moved greater distances than corresponding markers on the epicardial surface This is expression of the difference in the degree of shortening of the inner and outer layers of myocardial fibers (see Chapter 7)

The apex remained remarkably stationary in all studies of this type Rotation of the ventricles was slight or negligible Contraction of the right ventricular wall apparently acts primarily to draw the A-V valve ring toward the apex During left ventricular contraction the diameter of the cylindrical portion of the ventricular chamber was reduced and the long axis of the chamber shortened (Fig 11) Since the interventricular septum did not shorten significantly, *contraction of the right and left ventricular walls* may cause the mitral and tricuspid valve rings to swing up and down from a fulcrum at their mutual attachments to the interventricular septum (see Fig 1) In both ventricles the pins on opposite sides of the chamber remained widely separated at the *end of each systole, indicating that large* quantities of blood remain within the ventricle at the end of a systolic ejection (see also Figs 9, 13)

The Mechanisms of Ventricular Ejection

Blood is ejected from the right ventricle by three separate mechanisms occurring more or less simultaneously (Fig 12) (*a*) Contraction of the spiral muscles (Fig 3) draws the tricuspid valve ring toward the apex of the heart and shortens the longitudinal axis of the chamber Shortening of the chamber along this axis is the most obvious *movement, but is much less effective in* ejecting blood than the bellows action (*b*) The free wall of the right ventricle moves toward the convex surface of the interventricular septum This movement is very slight but extremely effective in ejecting blood (*c*) Contraction of the deep circular fibers enclosing the left ventricular cavity must produce a greater curvature of the interventricular septum (Fig 12), although the mid-portion (central axis) of this septum remains remarkably fixed in both position and length [4] Since the free wall of the right ventricle is attached to the left ventricle along the interventricular groove, traction on this wall will also contribute to the bellows action on the right ventricular cavity This effect is so slight that it cannot be readily demonstrated on cinefluorographic films However it has been clearly demonstrated that the free wall of the right ventricle can be almost completely destroyed by cauterization in dogs[13 15] or by coronary occlusion in man[16] without obvious immediate effects on the circulatory efficiency If right ventricular ejection can be maintained without contraction of the right ventricular myocardium, tension applied to the free wall of the chamber resulting from left ventricular contraction must be sufficient to account for the right ventricular output This mechanism could be effective only if very slight movements of the free wall of the right ventricle toward the interventricular septum displace very large volumes of blood from the right ventricular cavity

Clearly the configuration of the right ventricle is ideally suited to the ejection of large

tremendously dilated so that the surface area per unit volume is increased. In other words the left ventricle assumes some of the characteristics of the right ventricle when large volumes must be ejected during each stroke.

Clearly the anatomic and architectural characteristics of the ventricular chambers reflect the type of work which each must perform (see Fig. 7). By the same token the functional characteristics of the circulatory trees which they serve establish the nature of *the load or the working conditions* of each ventricular chamber. For this reason cardiac function in health and disease must be considered in relation to the functional characteristics of the systemic and pulmonary vascular systems.

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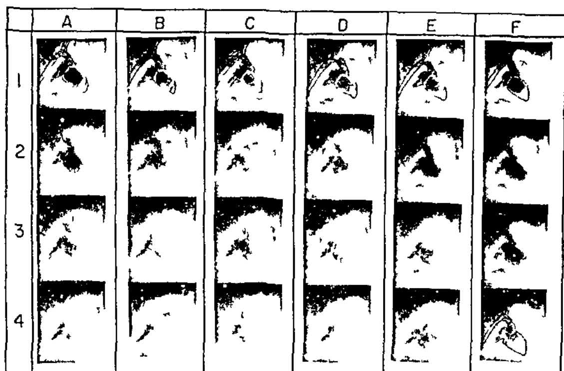


FIGURE 13 Left ventricular contraction is illustrated by cinefluorographic angiocardiography in normal dogs. The diameter of the chamber is considerably reduced and its *longitudinal axis is slightly shortened*. Systole began on frame *A* 3 and was completed on frame *C* 1. Diastolic filling appeared to be essentially complete in frame *D*-3 and little additional expansion could be noted during the remainder of the diastolic interval.

the longitudinal axis of the chamber. Contraction of the deep constrictor muscle bundles acts to reduce the diameter of the chamber (see Fig. 12). *This action accounts* for most of the power and volume of the ejection, since the volume contained decreases with the square of the radius in a cylinder (Fig. 12*B*). Shortening of the longitudinal axis is less prominent and less effective in ejecting blood because the volume *displacement is directly proportional to the* change in length. Changes in the size and configuration of the left ventricular cavity can be visualized by cinefluorographic angiocardiography (Fig. 13).

Shortening of the chamber involves movement of the mitral valve ring toward the apex of the heart (see Figs. 11, 12, 13). During diastole, the A-V junction rapidly ascends toward the left atrium. Since the interventricular septum shortens very little (Fig. 11), the distance between the root of the aorta and the apex of the heart changes very little. This observation is consistent with the conclusions drawn by Keith[17] that the ventricular myocardium contracts toward a fulcrum *or axis drawn between the apex of the heart* and the roots of the arterial trunks.

In contrast to the right ventricle, the left ventricular cavity has a small surface area in relation to the contained volume by virtue of its rounded, cylindrical contour. The thick cuff of deep myocardial bundles is ideally situated *to develop a very high internal* pressure during contraction. Thus the left ventricle is architecturally designed as a high-pressure pump which is consistent with its role of supplying energy for the flow of blood through the high-pressure, high-resistance, systemic circulation (see Fig. 7). The normal left ventricle has less adaptability than the right ventricle in ejecting large volumes of blood. When the left ventricle is exposed to an excessive *volume load for* extended periods of time, e.g., in aortic insufficiency, the chambers often become

by a schematic drawing in which all the capillaries in the body are arranged in parallel (Fig 1) All arterial branches having the same caliber are schematically arranged one above the other Similarly the corresponding branches of the venous system are vertically oriented In this way it is possible to demonstrate the effects of the branching arterial and venous systems on the pressure and flow of blood in corresponding segments of the circulatory tree

Volume Flow through Various Segments of the Circulatory System

The anatomic complexity of the peripheral circulatory distribution tends to obscure some very basic principles which are obvious in a single tube For example, if fluids flows into the single straight tube at the bottom of Figure 1 at a rate of 5 liters per minute, the same quantity of fluid must flow out of the tube Similarly 5 liters must flow past each of the vertical lines (A B C, D E) during each minute The only possible exception to this rule would result from a shift of fluid from one segment to another Such a redistribution of fluid would produce transient and relatively insignificant differences in the flow past the various regions of the tube A schematic representation such as Figure 1 shows the general applicability of this rule in the systemic circulation namely the quan

THE RELATION BETWEEN CROSS SECTIONAL AREA AND THE VELOCITY OF FLOW IN THE SYSTEMIC CIRCULATION

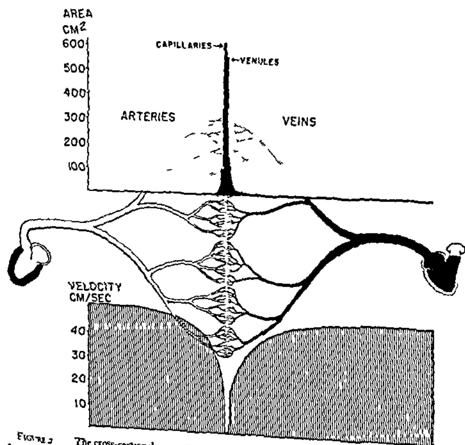


FIGURE 2 The cross-sectional areas of various segments of the systemic circulation have been computed for a 13 kg dog Note the tremendous area in the arterioles capillaries and venules The velocity of blood flow is inversely proportional to the cross-sectional area so that blood flows through the capillaries at about 0 07 cm./sec. (see reference 1)

Chapter 2

Functional Characteristics of the Systemic Circulation

The principal function of the heart is to convert stores of chemical energy into the mechanical work required to propel blood through the vascular systems. The useful work performed by the heart is determined by the quantity of blood ejected and the pressure developed during contraction. The magnitude of both factors is dictated by conditions in the circulatory beds served by the individual ventricles. The amount of useful work performed by the ventricle precisely balances the frictional loss of energy as the blood flows through the vascular tree. The present discussion will be limited to the hemodynamic characteristics of the systemic circulation as they affect the function of the left ventricle.

RAMIFICATION OF THE SYSTEMIC CIRCULATION

Blood pumped by the left ventricle must be distributed to the immediate vicinity of untold billions of cells in the body. This requirement is fulfilled by the diffuse arborization of the arterial tree by which a single arterial trunk gives off branches which in turn divide and subdivide to produce the complex ramifications of the arteries which deliver blood to all the millions of capillaries in the various tissues of the body. In the same way, blood which has traversed the capillaries returns to the heart by way of venous channels which have similar ramifications in most regions of the body. This complex circulatory pattern can be simplified

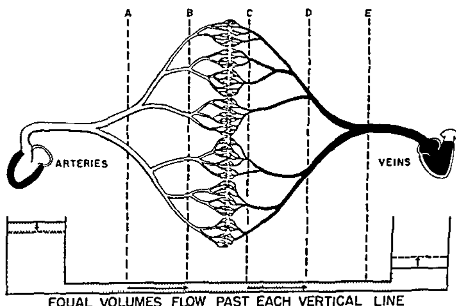


FIGURE 1. The arborization of the systemic circulatory system is schematically represented with all the vessels of the same caliber arranged vertically. This simplified illustration emphasizes the fact that the volume of fluid flowing past each of the vertical lines in unit time must be equal to the quantity entering and leaving the system, just as in a single tube.

enous blood only approaches and does qual that of the arterial blood It is ily necessary to distinguish between e flow and velocity of blood flow The e flow of blood through a particular depends upon the pressure gradient sistance to flow and the physical char stics of blood

stance to Blood Flow in the rculation (Fig 3)

id flows through tubes in response gradient in pressure The progressive tion in the pressure of fluid passing gh a tube of constant bore represents nergy which is lost as heat due to fric- The difference between the pressures e two ends of a tube is a measure of the tal loss of energy or of the resistance e flow of fluid For example consider a flow of water through the horizontal in Figure 3 A The pressure gradient is ted by the height of the columns of in the vertical tubes In passing through the segment labeled R the pressure drop is given as 1 cm of water While passing through the next segment where the radius is reduced to ½ R the pressure drop is 16 cm of water The frictional resistance as indicated by the pressure gradient is proportional to $\frac{1}{R^4}$ (the reciprocal of the fourth power of the radius) so that reducing radius by ½ increases the pressure drop sixteenfold

In a tube of constant bore the pressure drop is directly proportional to the length of the tube Thus if the length of the tube is doubled the magnitude of the pressure drop is also doubled (Fig 3B) The pressure drop is also directly proportional to the rate of flow (Fig 3C) Finally the pressure drop along a tube is directly proportional to the viscosity of the fluid The interrelationships of these factors have been combined in a formula (Fig 3D) which summarizes Poiseuille s law for streamlined flow of viscous fluids through rigid tubes

Poiseuille s law cannot be quantitatively

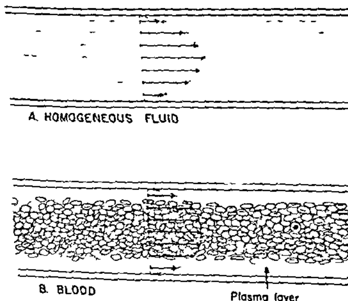


FIGURE 4. When a homogeneous fluid flows smoothly through a tube the layer immediately in contact h the wall does n t move wh le the inner l yers flow at progressively faster velocities toward the center of stream. When the velocity of flow is increased beyond some critical level, turbulence develops (see also Figure) The flow of blood is laminar in most portions of the circulatory tree The blood cells assemble in center of the stream and move more or less *en masse*

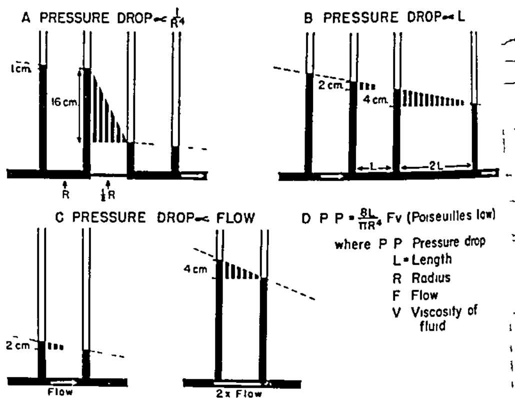


FIGURE 3 As a homogeneous viscous fluid flows without turbulence through rigid tubes of const caliber the pressure drop is determined by the radius of the tube the length of the tube the volume flow minute and the viscosity of the fluid as expressed by Poiseuille s law The most important factor is the rad of the tube (see text)

tity of blood flowing past each vertical line is exactly equal to the quantity pumped into the system and the quantity leaving the system per unit time except for slight and transient differences due to redistribution of the fluid volumes within the system It is true that the flow may be greater through one parallel channel than through another but the total flow through all corresponding segments must be essentially identical This very simple principle is neglected in many discussions of circulatory dynamics

Cross sectional Area of the Circulatory System (Fig 2)

When an artery or vein bifurcates, the cross-sectional area of its branches exceeds that of the parent vessel The number of vessels formed by this branching is so great that the estimated cross-sectional area of the capillaries is approximately 625 sq cm in a 13 kg dog with an aortic area of only c sq cm [1] Since the volumes of blood flowin through corresponding segments of th system are equal changes in cross section area affect the velocity of blood flow

Velocity of Blood Flow (Fig 2)

Just as water in a rushing stream slow down when it enters a broad pool so th velocity of flow is reduced in regions of th circulation with large cross-sectional area In the aorta blood travels at a velocity o 40 to 50 cm per second and in the capil laries it moves at about 0 07 cm per second Slow flow in the peripheral capillaries pro vides time for the exchange of material across the capillary walls After passing int the veins the blood again accelerates as th cross-sectional area progressively decreases However the caliber of the veins exceed that of corresponding arteries and the veloc

sense Since the arterial blood pressure and the length of the vessels tend to remain relatively fixed and the viscosity of the blood has limited variability the caliber of the vessels unquestionably plays a predominant role in determining both the pressure gradients and the flow through various segments of the circulatory system (Fig 5) The blood flows through the major arterial trunks with little frictional losses as indicated by the very sli ht gradients in the mean arterial pressure As the arteries divide and subdivide the caliber of the vessels diminishes and the pressure gradients become correspondingly steeper, particularly in the arterioles and capillaries Similarly the confluence of veins i associated with a reduction in resistance as blood flows from the capillaries toward the heart. In the larger veins blood flows briskly in response to very shallow pressure gradients The marked increase in resistance in the small vessels produces a precipitous fall in pressure which forms a functional line of demarcation between the arterial and the venous portions of the systemic circulation (Fig 5)

The volumes of blood contained within various segments of the systemic circulation are illustrated at the bottom of Figure 5 At any moment, the capillaries contain only about 5 per cent of the blood the arterial system holds only about 20 per cent and the remaining 75 per cent of the blood is accommodated by the capacious venous system

PRESSURE-VOLUME RELATIONS IN THE SYSTEMIC ARTERIES

The pressure in an elastic tube is an expression of the tension exerted by its walls Increased internal pressure can be attained by four mechanisms (*a*) increased distention by accumulation of fluid (*b*) active contraction of the walls without a change in contained volume (*c*) external compression and (*d*) the hydrostatic effects of continuous columns of blood

The pressure-volume relations of *isolated* segments of the arterial system are schematically presented in Figure 6 *A* If the arteries displayed purely elastic properties the arterial pressure would be determined solely by the volume of blood contained within them In other words so long as the mean arterial pressure remained constant the mean volume of blood within the arterial system would

PRESSURE-VOLUME RELATIONS IN ISOLATED ARTERIES

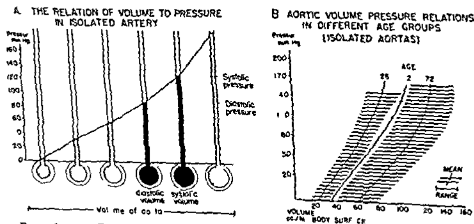


FIGURE 6 *A* The relation between volume and pressure in an isolated artery is illustrated schematically to emphasize the fact that as long as the distensibility of the wall remains constant, volume should always be the same at a particular pressure level.

B The pressure volume relations (distensibility) vary widely in different individuals in the same a e group although the curve tends to shift toward larger volume and less distensibility as subjects grow older (From Remington, Noback, Hamilton and Gold Amer J Physiol. 153 298–308 1948)

PRESSURES AND VOLUMES IN VARIOUS PORTIONS OF THE SYSTEMIC CIRCULATION

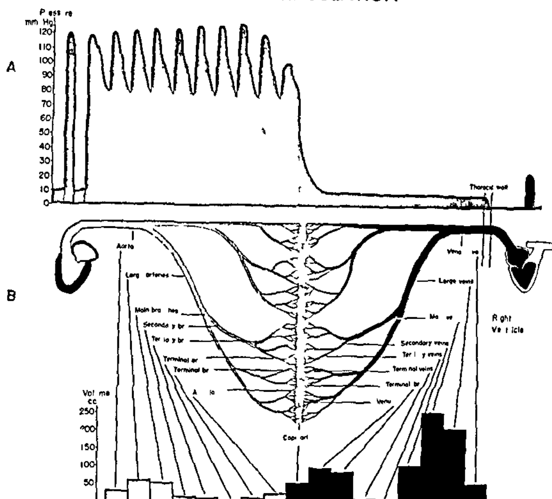


FIGURE 5 *A* The pressure drop is very gradual along the arterial tree to the terminal branches In the arterioles capillaries and venules the pressure gradient is very steep The pressure drop along the veins is slightly less than that of the corresponding arteries

B The capacity of the various segments of the systemic circulatory tree is illustrated to emphasize the fact that the veins accommodate a major portion of the total systemic blood volume (see reference 1)

applied to the circulatory system for several reasons (*a*) Blood vessels are not rigid, they stretch in response to an increase in pressure Elevated internal pressure may produce an increase in both radius and length For this *reason the pressure and the dimensions of* the tube are not independently variable (*b*) Plasma is a truly viscous fluid, but whole blood is not If plasma is perfused through an ordinary rigid tube, even the smallest differential pressure will produce some flow On the contrary when whole blood is perfused through the vascular system of an animal's extremity, no flow is produced until the pressure gradient from arteries to veins reaches some 10 mm Hg (even more in the presence of vasoconstriction) (*c*) Blood is not a homogeneous fluid since it contains large numbers of cellular elements which affect its flow through the vascular system *In most portions of the circulatory tree* the flow is laminar, but the presence of cells slows the flow in the center of the stream (Fig 4)

Pressure Gradients in the Circulatory Tree

While Poiseuille s law is not entirely applicable to the circulatory system the factors illustrated in Figure 3 apply in a qualitative

probably an expression of changes in the length of the vessel

The arterial system contains only about 20 per cent of the total blood in the systemic circulation (see Fig 5) Even if contraction reduced the volume of the arterial system by 30 per cent only some 250 to 300 cc of blood would be displaced The actual amount and significance of active constriction of the arteries is not known In general this system is considered to have a relatively constant volume so long as the arterial pressure remains fixed

Relatively small increments of volume change in the arteries produce large changes in pressure For example the arterial pulse wave at rest represents a large pressure fluctuation induced by the sudden injection of some 80 cc of blood into the central end of the arterial system In contrast a similar quantity of blood leaves the venous system at approximately equivalent rates during each cardiac cycle but the venous pressure varies only a few millimeters of mercury during each cycle This fact points up the principal differences between the relatively fixed-capacity arterial pressure reservoir and the variable-capacity, low pressure venous volume reservoir

The walls of the large arteries and veins are so thick and tough that their bursting pressure ranges in the thousands of millimeters of mercury Interposed between the arteries and veins lie the capillaries which have exceedingly small diameters and very thin walls Thin walls and small caliber are required in capillaries for the rapid diffusion of substances between the blood and tissues The mean internal pressure in arteries is normally about 100 mm Hg The delicate capillary walls support pressure amounting to 20 to 30 mm Hg at heart level and more than 100 mm Hg in the lower extremities while standing At first sight it is difficult to visualize how the fragile capillaries can support such very high internal pressures The explanation lies in the very small caliber of these vessels

The Relation between Pressure, Wall Tension and Caliber of Vessels

This relationship is graphically illustrated by a partially inflated rubber balloon[6] During inflation the mid portion of the balloon expands while the distal portion remains undistended (Fig 8) The portion of the balloon with a large radius is very tense and resists indentation indicating that the walls are under high tension The pressure is equal throughout the inside of the balloon and yet in the undistended region the walls are relatively flaccid and can be easily compressed[6] This commonplace example illustrates the law of Laplace ($T = P \times R$), which states that the tension in the wall of a hollow cylinder is directly proportional to the product of the tube's radius and the pressure being supported by the wall Burton[7] applying this law to the vascular system pointed out that an aorta with a radius of 1 3 cm supports a pressure of 100 mm Hg with a wall tension of 170 000 dynes per centimeter length (Fig 8) In

THE RELATION BETWEEN PRESSURE WALL TENSION AND RADIUS IN HOLLOW ORGANS

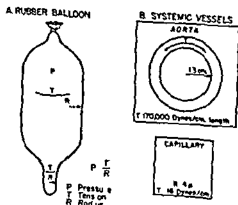


FIGURE 8 *A* In a partially expanded balloon, internal pressure is constant throughout, but the wall tension is very much greater in the distended portion than in the undistended tip because of the difference in radius As the radius increases, the wall tension must also increase to support a given pressure

B Because of the tremendous differences in radius the wall tension in the aorta is approximately 10 000 times as great as in a capillary even though they support similar pressures.

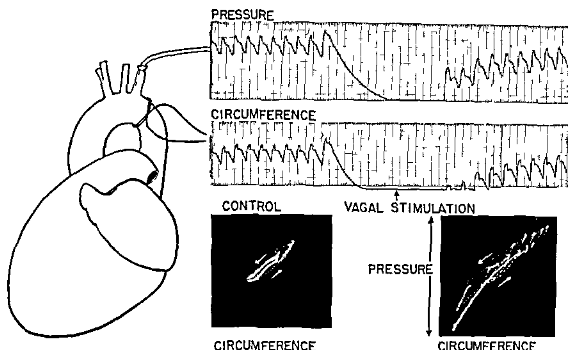


FIGURE 7 Simultaneous records of circumference and pressure in the same portion of the aorta are similar in contour Such records have been obtained from intact unanesthetized dogs for the first time The pressure-circumference relationships can be recorded continuously on a cathode ray oscilloscope by applying the output from the pressure recording device to the vertical plates and the output from the circumference gauge to the horizontal plates Under these conditions an increase in pressure deflects the beam upwards and an increase in circumference deflects the beam to the right Using the same equipment on simple rubber tubes the beam followed almost exactly the same sloping line during both expansion and deflation A similar response was obtained as the pressure and circumference diminished progressively when the heart was arrested by vagal stimulation However as soon as the heart began to contract the pressure-circumference relations formed a loop during each cycle

also be constant According to the distensibility curve in Figure 6*A*, pulse pressure should always be greater if the arterial pressure were increased while the stroke volume ramained the same The distensibility of the aorta varies widely in different individuals (Fig 6*B*) Further, the pressure-volume relationships in *isolated* arteries may not strictly apply to conditions in the intact animal or man because the caliber of the arteries may be actively reduced by contraction of the walls in response to an increase in arterial pressure[3] and by topically applied epinephrine [4] Indeed, there is some evidence that the distensibility of the aorta varies during each cardiac cycle [5]

If aortic pressure and aortic circumference are measured simultaneously, very similar patterns appear on the two records (Fig 7) This indicates *an intimate relationship* between the pressure and volume of the measured aortic segment

In a perfectly elastic tube, the pressure-volume relationships can be described as a single curve which is unaltered by the rate of distention or deflation Extensive investigation of the pressure-volume relations of isolated segments of arteries has revealed differences between the curve produced during distention and that recorded during deflation of the vessel (hysteresis) In Figure 7, the pressure-circumference loops are inscribed in counterclockwise direction, suggesting an energy gain in the system Since it is unlikely that the aorta actively contracts during part of each cardiac cycle, this is

of 12 A The total area of the 'pores is so small that they may *be localized to the spaces between* adjacent endothelial cells Renkin[12] presented evidence that lipid-soluble substances may diffuse through the capillary endothelium so that capillary exchange of oxygen and carbon dioxide may utilize the entire capillary wall

The Structure of Capillary Walls

Typical capillaries are thin walled tubes of endothelial cells The endothelial cells resemble fried eggs in shape and are only about 1μ thick except at the nucleus (Fig 9) These flat cells are joined at their edges by a substance called intercellular cement,'[13] *which* is visualized as composed of long chain molecules bridging the slit between adjacent cells Interstices between these molecules are considered responsible for the sieve-like properties of capillary walls and may correspond to the ' pores described above The endothelial tube is believed to be lined with a layer of colloid adsorbed upon its inner surface Surrounding the capillary tube is another membrane consisting of cells (pericytes) resembling fibroblasts intermingled with reticular fibers which completely surround the vessel[13 16] Between *the capillary wall and the* perivascular membrane is the perivascular space *which is* occupied by *a fluid which flows freely within* it (Fig 10) The perivascular membrane forms a line of demarcation between the fluid in the perivascular space and the gelatinous matrix in the interstitial spaces The so-called tissue fluid is largely bound in a gel *structure* resembling the familiar gelatin

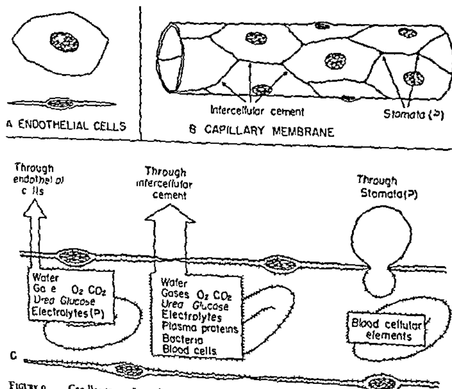


FIGURE 9 Capillaries are formed of *endothelial cells* joined at their edges by "intercellular cement" to form tubes. It seems likely that water gases small organic molecules and possibly certain electrolytes can pass through the endothelial cells. Most of the capillary *exchange probably occurs* through the *intercellular* cement (see text) *It has been* postulated that blood cellular elements pass through *orifices* between endothelial cells called stomata.

contrast, capillaries with a radius of 4μ support a pressure of some 30 mm Hg with a wall tension of only 16 dynes per centimeter length In other words, the pressure in the aorta is about three or four times as great as that in the capillaries while the radius is some three thousand times as great. Therefore, the wall tension in the aorta is about ten thousand times as great as that in the capillaries The breaking strength of lens paper or Kleenex is over three thousand times as great as the tension in the walls of capillaries at heart level In tubes of very small caliber, no great strength is required to support a high internal pressure By the same token, the capillary walls can be very thin so that the distance of diffusion from the central portion of the capillary blood to the outside can be very short These physical attributes of the capillaries are essential to *their function*

THE STRUCTURE AND FUNCTION OF CAPILLARIES

A major portion of the pressure drop between arteries and veins occurs at the points of controlled resistance at the entrance to the capillary channels (see Fig 5) In addition, a fairly steep pressure gradient along the capillaries is required to maintain flow because of their small caliber The velocity of blood flow is less in the capillaries than elsewhere because of their tremendous total cross-sectional area (Fig 2) For the same reason the total surface area of capillary walls is very extensive, particularly in relation to the quantity of blood within each capillary vessel and the total volume of the capillary beds, about 5 per cent of the total blood volume All the blood in the capillaries comes very close to the extravascular tissue spaces, a condition essential for the rapid transfer of substances by diffusion The movement of molecules in response to concentration gradients (diffusion) is a very slow process for long distances since the time of diffusion varies with the square of the distance For example, a nerve trunk 0 7 mm in diameter suddenly placed in oxygen would require about 54 seconds to reach 90 per cent saturation, but a cylinder of the same material 1 cm in diameter would require 11,100 seconds [8] Single nerve fibers 7μ thick would take only 0 0054 second Unaided by circulation or flow currents, a molecule would require more than one hundred years to pass from one end of the human body to the other The same molecule could cover a distance of 1 5μ in approximately 0 003 second Hill[8] has estimated that a capillary serves about twelve times its own volume of skeletal muscle, so the diffusion distances are small The functional significance of the wide-spread arborization of the vascular tree and the dense networks of capillaries (Fig 1) becomes clear when considered in this light

Ions and small molecules diffuse across the capillary walls at a surprising rate *Flexner and his associates*[9 10] *studied this* problem with radioactive tracers and concluded *that 60 per cent of the sodium in* plasma was exchanged for extravascular sodium in 1 minute Similarly 64 per cent of the chloride in plasma and 140 per cent of the water were calculated to be exchanged each minute [9] On this basis they believed that the whole capillary wall was permeable to these substances and that they moved through both the endothelial cells and the spaces between these cells

Using more quantitative techniques, Pappenheimer et al [11] obtained evidence that the amount of water and lipid-insoluble molecules transferred is some two hundred times greater than the values calculated by Flexner and his group They found that the area of the capillary walls available for diffusion of a molecule the size of water is less than 0 2 per cent of the total wall surface Ultramicroscopic holes or pores in the capillary wall with uniform diameters of 30 Angstrom units (A) account very well for the diffusion rates of fat-insoluble molecules ranging in size from that of sodium chloride to that of hemoglobin The data could also be explained by a range of pore dimensions with a mean of 24 A and a standard deviation

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STRUCTURE AND PERMEABILITY OF CAPILLARIES

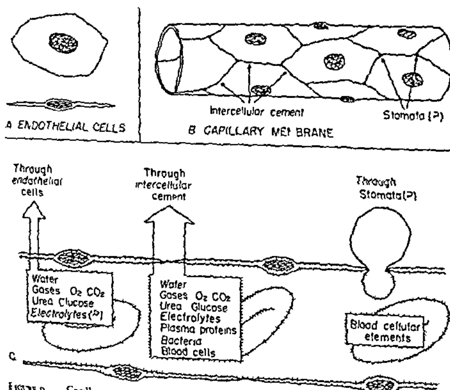


FIGURE 9 *Capillaries are formed of endothelial cells joined at their edges by "intercellular cement* to form tubes. It seems likely that water gases small organic molecules and *possibly certain electrolytes* can pass through the endothelial cells *Most of the capillary exchange probably occurs through the intercellular cement* (see text) It has been postulated that blood cellular elements pass through orifices between endothelial cells called stomata.

THE RELATION OF CAPILLARIES TO TISSUE SPACES

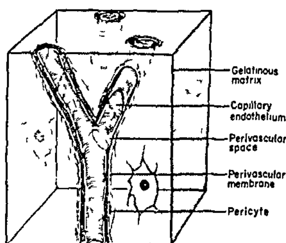


FIGURE 10 *In many tissues the capillaries lie within a space containing free fluid (perivascular space) surrounded by another membrane (perivascular membrane) which separates the perivascular fluid from the interstitial gel*

desserts Although this anatomic relationship has been demonstrated primarily in connective tissues, most of the body capillaries are distributed to the vicinity of the cells by way of the connective tissue stroma of the various organs Thus, the anatomic relationships illustrated in Figure 10 may obtain widely throughout the body, although this has not been clearly demonstrated

The perivascular membranes may afford a mechanical support for the capillary walls The presence of two membranes may account for the common clinical experience that changes in permeability and changes in capillary fragility occur independently Thus, changes in the capillary endothelium may be responsible for altered permeability, and failure of the perivascular membrane may result in increased capillary fragility, producing petechial hemorrhages Little is known

OSMOTIC PRESSURES IN BODY FLUIDS

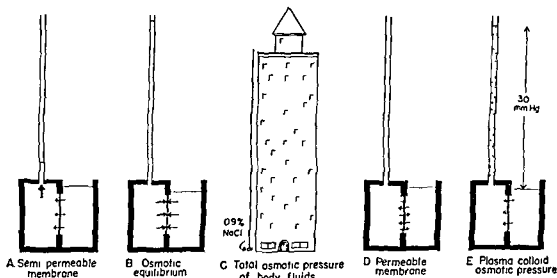


FIGURE 11 *A* When two solutions of different osmotic concentrations are separated by an appropriate semi permeable membrane fluid moves from the region of lower concentration through the membrane to dilute the solution with higher concentration

B Osmotic equilibrium is reached when the hydrostatic pressure in the vertical fluid column precisely balances the osmotic pressure exerted by the more concentrated solution

C The total osmotic pressure of any of the body fluids is about 7 9 atmospheres when equilibrated with pure water This pressure is equivalent to the vertical column of 0 9 per cent saline solution extending to the top of a 20-story building

D If solutions of different osmotic concentration are separated by permeable membranes no osmotic pressure is present at equilibrium because both the water and solutes diffuse to produce equal osmotic concentrations throughout the fluid phase For this reason the tremendous potential osmotic pressure of body fluid (*C*) serves merely to maintain osmotic equilibrium throughout the fluid compartments of the body

E Since the capillary walls are highly permeable to solutes other than *plasma proteins the osmotic pressure* of the plasma is determined by the difference in concentration of the proteins and amounts to only about 25 to 30 mm Hg

about the functional significance of the endocapillary layer, the perivascular membrane or the interstitial gel so the postulated mechanisms are generally described in terms of the characteristics of the capillary membrane alone

Water Balance at the Capillaries

Since water molecules move back and forth so rapidly between blood and tissues and the pressure inside the capillaries is greater than extravascular pressure why does water remain in the blood stream rather than pouring out into the tissues? If this occurred the blood volume would shrink and the blood would become so viscous that circulation would cease The fluid exchange across capillary walls was described by Starling[17] as follows

> In Lecture II I called your attention to the fact that the non-diffusible constituents of the blood serum, chiefly proteins were capable of exercising an osmotic pressure or osmotic attraction for water which amounted to about 4 mm. Hg for every 1 per cent protein in the serum. Blood plasma with 6 to 8 per cent proteins would therefore exert an osmotic pressure of 25 to 30 mm. Hg as compared with an isotonic salt solution The importance of these results lies in the fact that, although the osmotic pressure of the proteins of the plasma is so insignificant when contrasted with that of its saline constituents it is of an order of magnitude comparable to that of the capillary blood pressure [see Figure 11] and whereas capillary pressure is the chief determining factor in the production of interstitial fluid the osmotic difference of pressure dependent on the greater concentration of the fluid within as compared with that without the blood vessels might be sufficient to determine absorption. In fact the osmotic attraction of the serum, or plasma, for the extravascular fluid will be proportional to the forces expended in the production of the latter so that at any given time there may be a balance between the hydrostatic pressure of the blood in the capillaries and the osmotic attraction of the blood for the surrounding fluids. With increased capillary pressure there must be increased transudation. The blood will become more concentrated until equilibrium is established at a somewhat higher point, when there is a more dilute fluid in the tissue spaces and therefore a higher absorbing force to balance the increased capillary pressure. With diminished capillary pressure there will be an osmotic absorption of salt solution from the extravascular fluid this becomes richer in proteins, and the process will come to an end when the difference between its protein osmotic pressure and that of the intravascular plasma is equal to the diminished capillary pressure

According to this hypothesis the filtration or reabsorption of fluid across the capillary walls depends upon the net effect of four interdependent forces (*a*) capillary pressure (*b*) tissue pressure (*c*) osmotic pressure of

FACTORS DETERMINING FLUID EXCHANGE IN CAPILLARIES

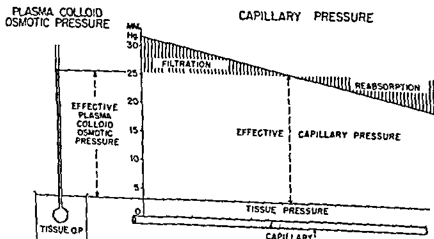


FIGURE 12 The effective colloid osmotic pressure of the plasma is determined by the difference in protein concentration in tissues and in the plasma. The effective capillary pressure is the difference between capillary pressure and tissue pressure. The pressure gradient in capillaries under a specific set of conditions may produce filtration at the arteriolar end of the capillary and reabsorption in the venular end of the capillary with no net fluid exchange. Such complete fluid balance is the exception rather than the rule

the plasma and (*d*) osmotic pressure of the tissue fluids For sake of convenience, the difference between capillary pressure and tissue pressure will be called *effective capillary pressure* or *filtration pressure* The difference between plasma and tissue osmotic pressure will be termed *effective plasma osmotic pressure* The maximal effective plasma osmotic pressure ranges around 30 mm Hg in regions where the capillaries are virtually impermeable to proteins The average effective capillary pressure is in this range at heart level Starling's hypothesis calls for a fairly complete balance of filtration and reabsorption in relatively impermeable capillaries at heart level when the mean *capillary pressure approximates effective* colloid osmotic pressure (Fig 12) Under these conditions, no filtrate or lymph would be formed

Capillary Permeability in Different Regions

The effective plasma osmotic pressure is markedly reduced in capillaries with greater permeability to protein Judging from the protein concentration of lymph from different regions capillary permeability is not uniform throughout the body (Fig 13) For example, lymph actively flowing from skin and connective tissues generally contains less than 1 per cent protein Lymph from heart, lungs, intestines and kidney usually contains protein in concentrations between 3 and 4 per cent Liver lymph carries as much as 6 per cent protein when the plasma concentration is only about 7 per cent, *suggesting* an effective colloid osmotic pressure of about 4 mm Hg in the liver sinusoids In tissues where protein escapes from capillaries in *concentrations of 3 per cent or more,* lymph flows continuously However, lymph is not universally *accepted as an example of tissue* fluid

RELATIVE PERMEABILITY OF CAPILLARIES IN VARIOUS TISSUES

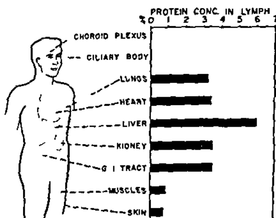


FIGURE 13 Under normal conditions the choroid plexus ciliary body and renal glomeruli are essentially impermeable to protein Capillaries in most of the viscera are relatively permeable judging from the protein content of lymph In muscle and skin the capillaries are but slightly permeable to proteins

Variations in Capillary Pressure

Most of the confirmatory evidence for Starling's hypothesis has been derived from *experiments on small animals with capillaries* at or near heart level [18] Clearly filtration is most likely to predominate in regions where marked elevation in capillary pressure *is not balanced by a corresponding increase* in extravascular pressure

Since fluid flows from regions of high pressure to regions of lower pressure, the pressure *in peripheral veins establishes the minimal* capillary pressure in each capillary network Similarly the filling pressure of the right ventricle establishes the lower end of the *shallow gradient in venous pressure* (Fig 5) Thus the capillary pressure is affected by changes in either local venous pressure or the diastolic pressure in the right ventricle

Some factors which affect capillary fluid balance are illustrated schematically in Figure 14 When humans stand up the long hydrostatic columns of blood tend to produce great increases in capillary pressure without corresponding increases in effective osmotic pressure of the blood This problem will be considered in the next chapter

THE VENOUS SYSTEM

The veins not only act as conduits to channel blood from the capillaries to the heart, but they also adjust their total capacity

FACTORS INFLUENCING FLUID BALANCE AT THE CAPILLARIES

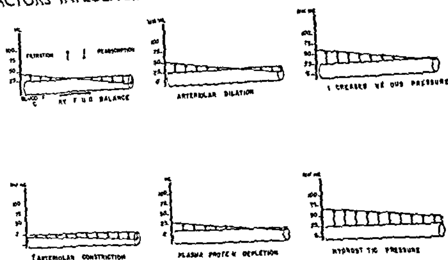


FIGURE 14. Filtration and reabsorption of fluid are balanced only when the effective plasma osmotic pressure precisely equals the mean effective *capillary pressure*. Dilatation of arterioles causes a *steeper capillary pressure gradient with little change in venous pressure*. Increased venous pressure and hydrostatic pressure in dependent parts elevates the *pressures* along the whole length of the capillary. Plasma protein depletion and increased capillary permeability reduce the tendency for reabsorption and foster excess filtration. Net reabsorption of fluid is aided by arteriolar constriction or by elevating the capillaries above heart level. (From Sodeman W. A. Pathologic Physiology Mechanisms of Disease Philadelphia W. B. Saunders Co.)

to accommodate variations *in total* blood volume. The pressure at the *point of outflow* from a system of tubes establishes *the lower* end of the pressure gradient which promotes flow through the tubes. The point of outflow from the systemic veins is the right ventricle during each diastole. If the *pressure* in the right atrium fell below the *pressure outside* the wall of this vessel the filling pressure of the right ventricle would be zero. Actually the pressure *within* the right atrium and ventricle remains within a narrow range at very low levels in spite of changes in the total blood volume or the distribution of blood in the circulation. The maintenance of a fairly constant right atrial and right ventricular pressure under varying conditions requires adjustments in the capacity of various portions of the venous system. Measurements on isolated segments of veins reveal smaller pressure increments with increasing volume than occur in arteries. The greater venous distensibility represents only part of the adaptability of the venous system. The variable capacity of the venous system is vested *in* specialized venous reservoirs and *in alterations* in the caliber of venous channels through venoconstriction.

Reservoirs of Blood

A large portion of the venous vascular bed has variable capacity under neural control. Franklin[19] *stated*: "In the body the musculature of the veins controls a large *part of* the venous system and associated blood depots and hence the *venous return* and heart minute volume. By virtue of a sphincter like action of the hepatic vein near its entrance into the inferior vena cava the blood content of the liver can be increased or diminished." Evidence has been presented that widespread constriction can occur over the distribution of the hepatic veins.[20] The tremendous enlargement *of the liver* accompanying right ventricular failure is a striking example of the variable capacity of this organ. At the same time impedance to outflow from the hepatic veins would also tend to foster accumulation of blood within the capacious splanchnic veins. Further the

mesenteric veins are among the most reactive and muscular in the body and there is evidence that they can be constricted and relaxed by neural mechanisms to accommodate varying amounts of blood [19] It has long been recognized that the spleen acts as a depot from which blood may be expressed in times of stress This function is not well developed in the human spleen since it contains only some 200 to 250 cc The subpapillary plexus of the skin has a potential role as a blood depot, but this function is intimately related to dissipation of heat In other words, release of this blood into the general circulation rarely occurs at the expense of temperature regulation The pulmonary veins are generally believed to have less distensibility than the systemic veins, but very likely play a role in cushioning transient differences in the output of the right and left ventricles Although measuring the capacity of internal organs is very difficult, there is some evidence that the capacity of the venous channels may also be controlled by "venomotor" activity [21,22] Variations in venous "tone" would contribute to adjustment in the capacity of the circulation in response to alteration in blood volume [23] The fixed pressure-volume relations of isolated veins (Fig 15*A*) do not apply to the intact circulation Instead, adaptability in the capacity of veins provides a mechanism by which the volume of the venous system can change within rather wide limits without corresponding changes in venous pressure (Fig 15*B*) The functional significance of this feature lies in the control of central venous pressure and will be discussed in the next chapter

SUMMARY

The systemic circulation consists of three functional divisions, the arterial pressure reservoir, the venous volume reservoir and the capillary networks The precipitous drop of pressure due to high resistance to flow through the arterioles, capillaries and venules forms the functional region of demarcation between the arterial and venous systems So long as the pressure difference between arteries and veins remains constant, the blood flow through the capillaries is determined by the resistance to flow through the minute

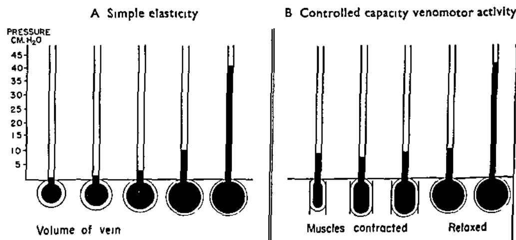


FIGURE 15 *A* The relation between the pressure and the volume of isolated veins differs from that of isolated arteries (see Fig 6) The veins accommodate relatively large volumes of fluid with very slight increase in pressure until the limits of elasticity are approached With very great distention the pressure rises to very high levels

B By virtue of controlled capacity the volume of blood contained within veins may be varied without corresponding changes in pressure (see text) The capacity of the venous system can be varied by active contraction of veins and of venous reservoirs or by external compression i e through contraction of surrounding skeletal muscle In this schematic drawing the adaptability in venous capacity is illustrated as though the control resulted solely from external compression

vessels The quantity of blood flowing per unit time through the arteries capillaries and veins must be identical except for insignificant differences in flow involved in shifting blood from one region to another The central arterial and venous pressures tend to remain fixed within relatively narrow ranges regardless of the total amount of blood flowing through the system per unit time (cardiac output) The average volume of blood in the arterial system tends to remain fairly constant so long as the mean arterial blood pressure is unchanged In contrast, the central venous pressure tends to remain relatively constant in spite of variations in the total quantity and distribution of blood through adjustments in the capacity of venous reservoirs Cardiovascular response to disease cannot be fully understood without consideration of the mechanisms by which the normal circulatory system adjusts to various conditions including changes in body posture, changes in regional blood flow and cardiac output

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Chapter 3

Circulatory Response to Arising

The cardiovascular system is generally studied in supine subjects or animals. Circulatory dynamics are most stable while the individual is lying down because many of the arteries and veins are horizontally oriented at or near heart level. When one stands upright, many of the arteries and veins are oriented vertically and large hydrostatic pressures are produced by the long, uninterrupted columns of blood. The arterial, capillary and venous pressures are markedly elevated in the dependent extremities and the circulatory system must promptly make appropriate compensatory adaptation.[1,4] If these compensatory mechanisms are insufficient or retarded, orthostatic hypotension results. Fainting reactions in erect subjects are frequently produced by stimuli which would have virtually no effect on the supine individual. Recognition that a major portion of man's effective existence is spent in the erect position makes it appropriate to consider the cardiovascular adjustments required in this position.

VASCULAR PRESSURES IN RECLINING SUBJECTS

When the long axis of the body is horizontal, the long columns of blood are at or near heart level. The mean pressure throughout the entire systemic arterial tree is fairly uniform except for the slight pressure gradients incident to the frictional energy loss during flow through these tubes (Fig. 1, and

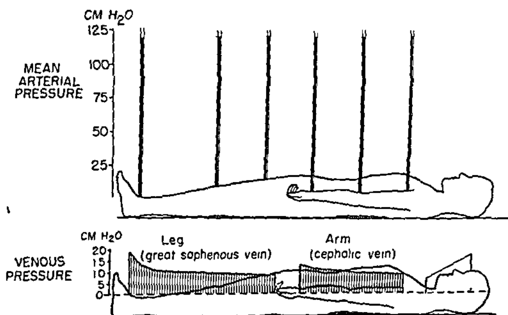


FIGURE 1. *A*. The mean arterial pressure diminishes but slightly from the arch of the aorta to the arterial branches, i.e., the radial. This pressure gradient is responsible for the flow of blood through the system. *B*. The peripheral venous pressure also has a very gradual diminution in pressure from the periphery toward the heart. In the smaller venous branches the pressure gradient is *considerably steeper*. (After Ochsner et al.[5])

see Chapter 2) The mean arterial pressure diminishes only a few millimeters of mercury during flow of the blood from the aorta to arterial branches the size of the radial artery at the wrist In the same way the venous pressure declines only slightly between the smallest venous branches in the extremities and the large central venous channels Venous pressure in peripheral veins of various caliber was measured at various points over the body surface by Ochsner et al[5] their data are schematically illustrated in Figure 1B Note that the pressure in the smallest peripheral veins averaged about 17 mm Hg in the lower extremity and that capillary pressure must exceed the pressures in the corresponding veins

PRESSURES PRODUCED BY HYDROSTATIC COLUMNS

The pressure in a rigid tube containing a continuous column of stationary fluid is determined by the vertical distance from the point of measurement to the top of the

THE NATURE AND SIGNIFICANCE OF HYDROSTATIC PRESSURES

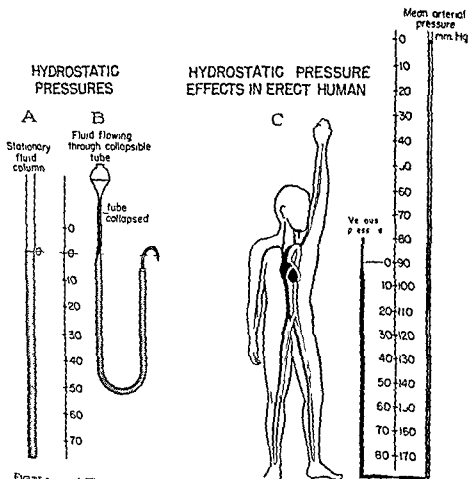


FIGURE 2 *A* The pressure in a column of fluid is dependent upon its specific gravity and the vertical distance from the point of measurement to the meniscus

B A collapsible tube is distended only so long as the internal pressure exceeds the external pressure These two pressures are exactly equal in the portion of the tube which is collapsed

C In the erect position the arterial and venous pressures are both increased by some 85 mm Hg at the ankle. With the arm elevated over the head the arterial pressure at the wrist is about 40 mm Hg and the effective venous pressure is zero down to a level just above the heart.

fluid (Fig 2A) At lower levels within the tube, the pressure in the fluid progressively increases owing to the action of gravity on the column of fluid above each point of measurement Strictly speaking, the meniscus of the fluid represents an interface between the fluid medium and the atmosphere, so the total magnitude of the pressure equals the hydrostatic pressure in the fluid column plus the ambient atmospheric pressure In the present discussion the hydrostatic pressure will be considered in relation to the specific gravity of the fluid and the vertical distance from the point of measurement to the level at which fluid pressure equals pressure immediately outside the tube

The venous system consists of a series of collapsible tubes so there is no interface between the venous blood and the external environment of the vein *If* at any point along the vein, venous pressure equals the external tissue pressure the vein collapses at *that level If* a *thin-walled* tube containing no air is arranged as indicated in Figure 2*B*, the fluid from the reservoir will flow through *the tube in response to a pressure gradient* The tube collapses at a level just above the outflow tube Below this level, the internal *pressure exceeds the external pressure and* the tube is distended by hydrostatic pressures which increase progressively toward the *lower portion of the system Above the zero* level, the pressure within the collapsed tube is equal to the external pressure Technically, a free-falling body has no weight because all the potential energy is converted into kinetic energy (movement) or lost as friction (heat) Thus, even though there is fluid flowing through the collapsed portion of the tube, the lateral pressure exactly equals the external pressure If a normal man assumes a semi-reclining position with his head and trunk oriented about 30 to 45 degrees from the horizontal plane, the lower portion of the jugular vein is distended, but at some point along its course it becomes collapsed because venous pressure equals tissue pressure This represents *the level of zero effective venous* pressure

When a normal man is standing, the level of zero effective venous pressure is within the thorax (Fig 2*C*) If there is a continuous column of blood extending from the foot to heart level, the pressure in an ankle vein should be about 85 mm Hg (125 cm H_2O) It has been demonstrated experimentally that this is approximately true so long as the subject remains relaxed and motionless Similarly, if the mean arterial blood pressure at heart level is 90 mm Hg the arterial blood pressure at the ankle should be increased by a corresponding amount, i e, to about 175 mm Hg, neglecting the slight frictional losses during flow indicated in Figure 1 Since the arterial and venous pressures in dependent extremities are increased to the same extent by hydrostatic pressure, the energy lost during circulation through dependent parts is no greater than that lost when the same vascular bed is at heart level The pressure differences between arteries and veins at the ankle are the same as *those* at heart level The frictional energy loss along a tube is not increased when it is *formed into a U tube* For example, *the* pressure head is the same for tubes *A* and *B* in Figure 3 and the flow from each tube is *essentially identical Forming a tube into* a dependent loop does not increase the amount of energy required to propel fluid through the *tube Thus, the erect position does not re*quire an increased energy output by the heart, but capillary pressure increases tremendously in the dependent parts of the body

COUNTER PRESSURES OPPOSING HYDROSTATIC PRESSURES

It is obvious that a capillary pressure exceeding a venous pressure of 85 mm Hg must also greatly exceed the maximum colloid osmotic pressure of the plasma proteins (about 30 mm Hg) *If the effective capillary* pressure throughout the vascular networks of a region significantly exceeds the maximal *colloid osmotic pressure, filtration of fluid* will occur from all parts of the capillary

THE EFFECTS OF DEPENDENCY ON THE FLOW OF FLUID

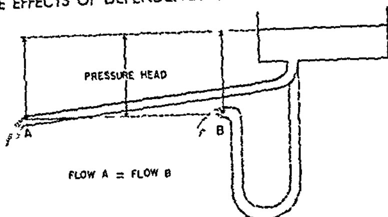


FIGURE 3 This simple model illustrates the point that assuming the erect position per se places no additional burden upon the heart. Since the frictional energy loss is essentially the same the same energy release (pressure head) provides equal flow from *A* and *B*

system reabsorption will be impossible and accumulation of fluid in the tissue spaces (edema) can result It is important to consider the extent to which this kind of situation is alleviated in various regions of the body by such mechanisms as (*a*) the balancing of intravascular pressures by extravascular or tissue pressure (*b*) the reduction in hydrostatic columns in veins by pumping action and (*c*) the return of unabsorbed capillary filtrate to the circulation by way of the lymphatic system

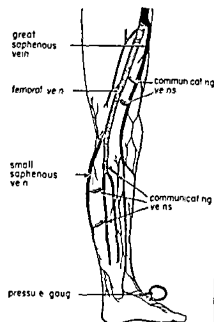
Intramuscular Tissue Pressure

In reclining subjects the intramuscular pressure ranges from 2 to 5 cm H_2O in muscles with loose fascial investment[6] i e, biceps brachii and gastrocnemius Slightly higher values have been obtained from anterior tibial and soleus muscles which are invested with a tight fascial sheath After being tilted into the erect position intramuscular pressures rise abruptly a few centimeters of water and then gradually increase to values of 20 or 30 cm H_2O in muscles with tight fascial covering Maximal pressures developed during voluntary muscular contraction are rarely reported over 50 cm H_2O although the venous pressure in the legs exceeds this amount[7,8] Muscles without tight fascial sheaths develop only relatively slight increases in pressure during maximal voluntary contraction For example, pressure in the rectus femoris could not be raised above 20 cm H_2O by maximal effort[6] Although the recorded values for intramuscular pressure are surprisingly low muscular contraction has important cardiovascular significance A relationship between low intramuscular pressure and syncope has been demonstrated by Mayerson and Burch[8] and by Gunther et al[9] Even more impressive is the fact that voluntary muscular contraction can apparently force blood under a cuff inflated to levels of 90 mm Hg[10] By some unknown means contraction of skeletal muscle in the legs is sufficient to compress the veins of the legs even when their internal pressure is very high This is the basis of a muscular pumping mechanism by which venous pressure in dependent extremities may be significantly lowered during the ordinary process of walking or shifting position

MUSCULAR PUMPING MECHANISMS Veins of the extremities are equipped with many valves located at strategic positions along their course So long as blood flows continuously throughout the peripheral venous system the valves are open along all the venous channels and the columns of blood are not interrupted at any point Under

PUMPING ACTION OF MUSCLES DURING WALKING

A COMMUNICATIONS BETWEEN SUPERFICIAL AND DEEP VEINS



B THE REDUCTION OF VENOUS PRESSURE DURING WALKING

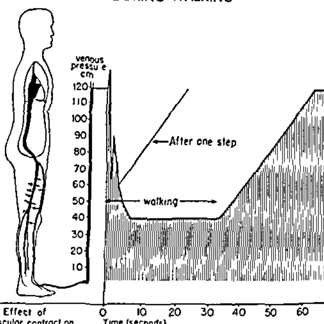


FIGURE 4 *A* Venous blood may ascend the leg along both deep and superficial channels which are in communication at many points To reduce the venous pressure at the ankle each of the vertical columns of blood draining the area must be interrupted at some point in the leg

B After taking one step the venous pressure in a dorsal vein of the foot is markedly reduced and then gradually ascends to the control level repetitive steps keep the venous pressure depressed (after Pollack and Wood[11])

these conditions the venous pressure at the dorsum of the foot is equivalent to a vertical column of blood extending from the point *of measurement to heart level (Figs 2, 4)* If the subject takes one step (Fig 4), the venous pressure at the ankle drops to a level *equivalent to a column of fluid extending to* the knee and then gradually returns to the previous level at a rate determined by the volume flow of blood through the extremity [11] There are alternate pathways by which blood from the foot may ascend the leg If any single uninterrupted column of blood from ankle to heart persisted after the step the venous pressure at the dorsum of the foot would not be altered Thus muscular contraction must produce complete or partial emptying of both the deep and superficial veins within the leg or thigh As the muscles relax, *the overlying columns of* blood are supported by closed intravenous valves According to Hojensgard and Sturup [12] the pressure in the deep and superficial leg veins may be reduced simul*taneously during walking The superficial* veins must empty into the deep veins of the thigh so that all the veins above the knee are *decompressed* This could be accomplished by complete emptying of veins or by segmenting the columns of blood so that each valve in the thigh is closed and supports a column of blood which does not extend to the valve above As blood flows through the capillaries into the veins the partially collapsed deep and superficial veins gradually refill elevating the pressure at the dorsum of the foot back to the initial levels Repeti*tive movements of the lower extremities* as in walking maintain the venous pressures at the lower level (Fig 4) if each successive step occurs before the venous columns in the thigh are refilled

This muscular pumping mechanism has important functional connotations (*a*) It drastically lowers the venous and capillary pressures reducing the effective capillary filtration pressures (*b*) It reduces the volume of blood contained within the veins of the leg and to this extent these veins act as a reservoir which releases excess blood during muscular exercise (*vide infra*) (*c*) It momentarily accelerates the return of venous blood from the legs at the onset of walking or running After the pumping mechanism is established the rate of venous return again depends upon the rate of blood flow through the capillaries into the veins When venous blood flows upward from the leg into the abdomen the pressure in the veins of the thigh must exceed the pressure in the abdominal portion of the inferior vena cava which has no valves In general the veins within the abdomen are filled with uninterrupted columns of blood under a pressure equivalent to that of a vertical column extending slightly above heart level

Intra abdominal Pressure

The abdominal cavity is filled with organs having a specific gravity approximating that of blood The hydrostatic pressure of a vertical column of abdominal organs is similar (Fig 5) to that which would be produced if the abdomen were filled with fluid 13 15 At rest the venous pressure apparently exceeds the intra abdominal pressure by only 5 to 10 cm H O at any level within the abdomen in either the supine or the erect position However the diaphragm and the abdominal walls may simultaneously exert tension during deep inspiration or straining so that the over all intra abdominal pressure exceeds venous pressure in the thorax and compresses the abdominal veins Blood is forced onward into the veins of the thorax because retrograde flow out of the abdominal cavity is prevented by closure of venous valves Since the diaphragm can exert no force in the upward direction intrathoracic pressure never exceeds intra-abdominal pressure

TRANSMURAL PRESSURES OF ABDOMINAL VEINS

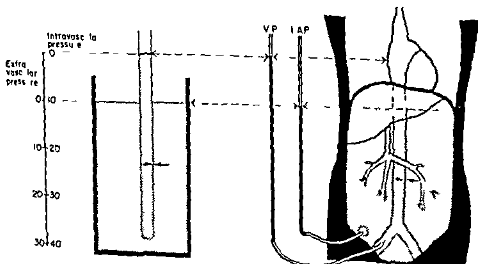


FIGURE 5 If a collapsible tube is filled with fluid and suspended in a tank of water the walls must support only the difference in pressure between the inside and the outside In the case illustrated the walls of the tube support no more than 10 cm H_2O pressure at any level in the tube. The abdomen contains movable organs with a specific gravity similar to that of blood For this reason the transmural pressure of intra abdominal veins is less than 10 cm H_2O at any level in the abdominal cavity

Intrathoracic Pressure

The collapsed volume of the lungs is much smaller than the capacity of the thoracic cage. *Since the lungs are stretched or distended to* fill their allotted space, the elastic tissue is *under stretch even at the end of a forced* expiration. This elastic tension of the pul*monary tissue is expressed as a subatmos*pheric intrathoracic pressure which exerts a distending *force on the structures within the* chest. An elastic tube filled with fluid is further distended if the tube is *confined* within a chamber containing a subatmos-

TRANSMURAL PRESSURE
IN THE THORAX

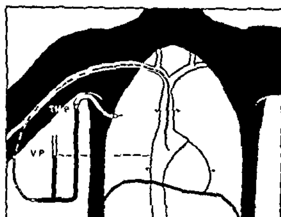


FIGURE 6. The central venous pressure recorded *with a catheter approximates atmospheric* pressure. The transmural pressure of the intrathoracic vessels is actually represented by the combined *effects of intrathoracic and intravascular* pressures. The intrathoracic pressure exerts a distending influence on vasculature within the thorax.

pheric pressure. The level of zero transmural *pressure occurs at the point at which the* internal fluid pressure is balanced by the *extravascular pressure*. The central venous pressure measured by a catheter ranges slightly above or slightly below the atmospheric pressure. However, the transmural pressure of the veins and atria is greater than the recorded values because of the subatmospheric pressure in the thorax. If the negative intrathoracic pressure is applied to the top of an external fluid column connected to an intrathoracic vein *(Fig. 6), the top of* the fluid column is elevated by the "suction" *of the subatmospheric intrathoracic pressure*. The "effective" venous pressure within the chest is indicated by such a manometer. The distending influence of the subatmospheric intrathoracic pressure tends to increase the transmural pressures throughout the thoracic cavity. It augments the central venous pressure in distending the large veins and the heart, reducing, to this extent, the lower end of the pressure gradient from the periphery to the right ventricle.

The intrathoracic pressure fluctuates during normal respiratory activity, averaging about -5.4 cm H_2O (-4 mm Hg) at the end of a normal expiration. Inspiration further distends the lungs, lowering the pressure to about -10.8 cm H_2O (-8 mm Hg). *Increased respiratory excursions pro*duce correspondingly greater fluctuations in *the intrathoracic pressure. Changes in intra*thoracic and intra-abdominal pressure asso*ciated with diaphragmatic movements pro*vide a pumping mechanism which facilitates transfer of blood into the thorax.

THE ABDOMINOTHORACIC PUMPING MECHANISM. During inspiration, the contracting diaphragm descends and the intrathoracic pressure is lowered by increased stretch of the inflated lungs. Simultaneously, the abdominal organs are displaced downward and forward; this displacement tends to stretch the anterior abdominal wall and *increases the over-all intra-abdominal pres*sure. Thus during inspiration, the gradient *in pressure between the abdomen and the* thorax is increased and blood flow into the *thoracic veins is accelerated (Fig. 7).* In addition, the shortening of the inferior vena cava reduces its capacity, contributing to the blood flow into the thorax.[16] The increased intra-abdominal pressure temporarily impedes *flow from the periphery into the ab*domen until the intra-abdominal pressure *is lowered during the subsequent expiratory* movement.

*Exhalation releases tension within the in*flated lungs and the intrathoracic pressure *rises toward atmospheric pressure*. Intra-abdominal pressure is reduced as the diaphragm relaxes and ascends. The inferior

vena cava becomes elongated and accommodates more blood[16] Thus blood flow from abdomen to thorax is accelerated during inspiration and slowed during expiration If expiration is continued beyond the normal range by active contraction of the abdominal muscles the diaphragm is stretched as it is elevated beyond the position of rest so that intra abdominal pressure is increased more than intrathoracic pressure rises Since the great importance because the transmural pressure in these veins represents the distending pressure of the heart A positive effective filling pressure must be maintained in these veins at all times regardless of the position of the body the magnitude of the blood volume, the redistribution of blood in dilated capillary beds or the accumulation of blood in distended dependent veins Otherwise, filling of the heart would be deficient

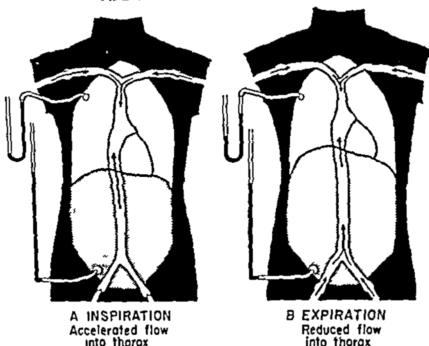


FIGURE 7 *A* During inspiration reduced intrathoracic pressure coupled with increased intra-abdominal pressure accelerates the flow of blood from the abdominal veins into the thorax.
B During expiration flow into the thorax is retarded by simultaneous increase in intrathoracic pressure and reduction in intra-abdominal pressure

diaphragm applies force only toward the abdominal cavity and elastic tension in the lungs is continuously present intra-abdominal pressure always exceeds intrathoracic pressure By this mechanism, a favorable pressure gradient from abdomen to thorax is always maintained under normal conditions

CONTROL OF CENTRAL VENOUS PRESSURE

The pressure in the intrathoracic portions of the superior and inferior venae cavae is of during the diastolic intervals On the other hand excessive pressure in these veins would raise the gradient in pressure in both the venous and the lymphatic systems, which would promote accumulation of fluid in the tissues The maintenance of central venous pressure between these two critical levels requires that the venous system compensate for variations in total blood volume and changes in its distribution[17 18] The right ventricular pressure during diastole represents the minimal pressure in the systemic

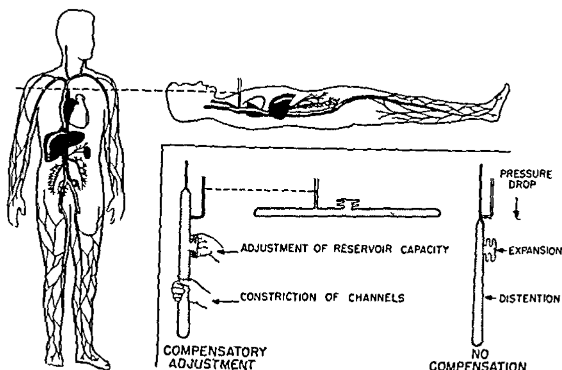


FIGURE 8 The veins in various regions of the body tend to be distended to about the same degree when a subject is recumbent In the erect position the hydrostatic columns of blood produce distention of the vessels below the heart and collapse of veins above the heart Since most of the venous reservoir capacity is below heart level the central venous pressure theoretically could fall below heart level unless compensatory adjustments were promptly instituted These compensatory mechanisms are illustrated schematically as a constriction of venous channels and regulation of reservoir capacity (see also Chapter 4)

venous system, since it is the point of outflow from the entire system At rest in the horizontal position, the right ventricular pressure varies between +2 and −2 mm Hg during *diastole Angiocardiographic studies*[19] have revealed that, in the supine position, both the superior and inferior venae cavae are distended with blood In the erect position, the inferior vena cava is distended, but the superior vena cava is partially collapsed just above the level of the right atrium The point of collapse of the veins represents the level at which the effective venous pressure (intravascular pressure − extravascular pressure) is essentially zero If the pressure in the inferior vena cava fell until the point of collapse was just below the right atrium, the effective filling pressure of the right ventricle would be zero Thus a decrease in venous pressure of only a few centimeters of water in the right atrium would represent a serious impairment of right ventricular filling This contingency is prevented by continuous and precise adjustments in the venous reservoir system to maintain the central venous pressure at levels only slightly above that of the right atrium *regardless of the body s position*

The mechanism which controls the central venous pressure is best described by a schematic diagram (Fig 8) Consider a distensible tube filled with water until there is a slight positive internal pressure when it is horizontal In the vertical position, the fluid level in the tube would descend because the hydrostatic pressure would produce greater distention of the dependent portions The fluid level could be restored to the previous height only by compression of some portion of the tube (Fig 8) Exactly the same considerations apply whether the fluid is stationary or is flowing through the tube (see Fig 2) The central venous pressure is only slightly above atmospheric pressure in normal re-

clining subjects When the individual assumes a vertical position the hydrostatic pressures produce a distention of the dependent veins which may accumulate relatively large quantities of blood (more than 500 cc.) Unless some portions of the venous vascular bed were compressed effective central venous pressure would probably fall below that of the heart A major portion of this blood may come from the lungs (see Chapter 4) However external compression of veins by skeletal muscles in the legs and probably by contraction of large venous channels and other venous reservoirs restores the central venous pressure to a level just above that of the right atrium The exact mechanisms controlling this important adjustment have not yet been elucidated

The probability that central venous pressure is precisely controlled was strengthened by exposing animals to positive and negative radial acceleration on a large centrifuge[20] Under forces as great as 5 times the force of gravity (5 g) pressures in dependent regions became elevated to very high values but the level at which venous pressure remained essentially unchanged was at or near heart level whether these forces were directed toward the head or toward the lower parts of the body (Fig 9) Since the capacity of the veins below the diaphragm greatly exceeds that of those above the diaphragm the

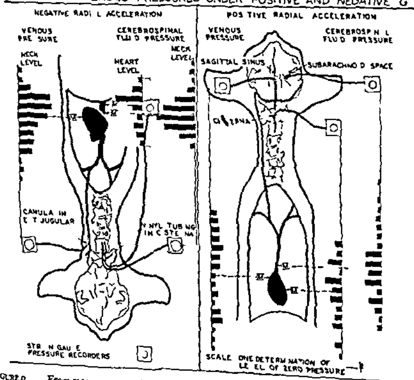


FIGURE 9 *From* measurements of venous and cerebrospinal fluid pressures the levels at which no change occurred were computed and plotted as a frequency distribution. The levels of minimal change in both pressures clustered about heart level during radial acceleration which produced forces as great as five times the force of gravity

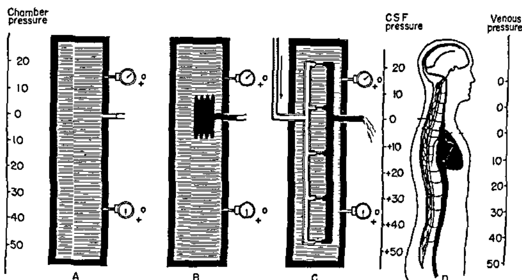


FIGURE 10 In a rigid container filled with fluid the pressure at the level of the horizontal tube equals atmospheric pressure Below this level the pressure progressively increases owing to the hydrostatic column of fluid Above the reference level the pressure progressively diminishes below atmospheric pressure This situation is unaltered by the presence of a distensible barrier between the contents of the chamber and the outlet tube If fluid flows into the chamber through rigid tubes and out through collapsible tubes the pressure within the collapsible tubes is precisely equal to the pressure outside the tube at any level within the rigid system By the same token the venous pressure determines the cerebrospinal fluid pressure within the cerebrospinal cavity

large hydrostatic pressures would tend to cause massive accumulations of blood in dependent regions when the forces acted from head to feet Control of central venous pressure must certainly involve regulating the capacity of the venous reservoirs

PROTECTION AFFORDED THE CEREBRAL CIRCULATION

Whenever a man is erect, the pressure in the cerebral cavity drops well below atmospheric pressure while in the lower spinal canal it is well above atmospheric pressure It has long been recognized that cerebrospinal fluid pressure varies with central venous pressure and affords protection to the cerebrospinal vascular bed The experimental data illustrated in Figure 9 indicate the intimate relation between venous and cerebrospinal fluid pressures [20] The cerebrospinal fluid pressure and the cerebral venous pressure vary together because they are confined within a relatively rigid chamber (Fig 10) If the analogy between the simple hydraulic models and the conditions in the cerebrospinal cavity is correct, the intravenous and extravenous pressure must be precisely equal at all levels of the cerebrospinal cavity regardless of its position or orientation Under these conditions the transmural pressure of veins is essentially zero and the effective capillary pressure is varied only by vasoconstriction or vasodilatation Under these conditions, the fluid balance postulated by Starling probably obtains in all the cerebrospinal capillaries except the choroid plexus and within the arachnoid villi An analogous situation obtains in the eye

SUMMARY

In the erect position, the arterial and venous pressures recorded at the ankle are both increased by as much as 85 mm Hg in an adult of average height The pressure

difference between arteries and veins remains unchanged and the energy release by the heart is no different from that in the supine position so long as muscular exertion is not required In fact the cardiac output has been reported to be slightly less when the subjects are relaxed in the upright position than when they are supine The major circulatory change produced by the hydrostatic columns is an increase in capillary pressure in dependent extremities This pressure reaches levels well above the maximum effective colloid osmotic pressure Contraction of the leg muscles during walking brings into play the so-called muscular pumping action which has three effects (a) At the beginning of muscular contraction blood is displaced from the veins of the legs owing to external compression (b) The pressure in the veins and capillaries in the lower extremities tends to be maintained at lower levels during active walking (c) The arteriovenous pressure difference is increased so that blood flow through the capillaries into the veins would be increased if the state of arteriolar constriction remained unchanged The quantity of blood flowing through the veins depends upon the rat of flow through the capillaries

The external pressure provided by the hydrostatic column of abdominal organs tends to balance the hydrostatic pressures in the veins of the abdomen By this mechanism, the vast splanchnic venous bed is largely protected from being distended by the increased venous pressures developed in the erect position The subatmospheric pressure within the thorax provides a favorable pressure gradient from abdomen to thorax Contraction of the diaphragm can act only to increase intra abdominal pressure and reduce intrathoracic pressure

The effective or transmural pressure in the thoracic veins atria and ventricles is greater than that recorded externally because the subatmospheric pressure acts as a distending force The filling pressure of the right ventricle is normally maintained at very low and constant levels by adjustments in the capacity of the venous reservoir system to compensate for variations in the distribution of blood and in the total blood volume

Changes in the position of the body have no functional effect on the vasculature within the cerebrospinal cavity and the eye and probably not in bone because the extravascular pressure precisely balances the venous pressure

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Chapter 4

Functional Characteristics of the Pulmonary Circulation

The systemic and pulmonary vascular beds are connected in series to form a continuous circuit Although these two vascular systems are superficially similar important differences between them should be kept in mind (*a*) The systemic circulation is a high-resistance circuit with a large difference in pressure between the arteries and veins, *while* the pulmonary circuit normally offers very slight resistance to flow (*b*) The pulmonary vessels supply only one type of tissue (alveolar membranes) so the requirements for vasomotor control are not as great as those in the systemic circulation (*c*) The volume of blood in the pulmonary system is neither so great nor so variable as that in the systemic circulation (*d*) Since the lungs immediately enclose the heart hydrostatic columns are fairly short even from the most distant portions of the pulmonary parenchyma (*e*) The pulmonary circulation is confined within the thoracic cage so extravascular conditions are fairly uniform throughout

ANATOMY OF THE PULMONARY CIRCULATION

The ramifications of the pulmonary arterial system closely parallel the arborization of the bronchial system The *mainstem* bronchi give off lateral branches which divide and subdivide like the branches of a tree At the tip of each terminal branch is a bronchiole which divides into two *respiratory* bronchioles These in turn divide into two branches each of which gives off three alveolar ducts The alveolar ducts are connected through a variable number of atria to a tuft of alveolar sacs (air cells) Gaseous interchange between the air and blood may occur in all divisions beyond the bronchioles

Structurally, the main pulmonary arteries closely resemble the aorta The walls of the main arteries and their branches remain essentially the same down to the intrapulmonary branches with outside diameters of about 1 mm except that the amount of smooth muscle in the wall progressively increases in the smaller branches[1] Muscular arteries ranging in diameter from 1 to 0 1 mm have a prominent *media of circularly* arranged smooth muscle between the internal and external elastic *laminae* The walls of arterial branches less than 0 1 mm in diam-

CAPILLARIES SUPPLYING RESPIRATORY MEMBRANES

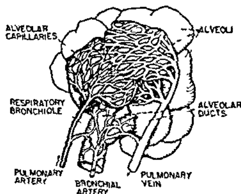


FIGURE 1 The *terminal* branches of the pulmonary artery enter directly *into* widely anastomotic alveolar capillary networks which are not equipped with true *muscular* arterioles or precapillary sphincters In the *respiratory* bronchioles the pulmonary and bronchial arterial branches serve the same capillary networks These common capillary beds drain into the pulmonary veins

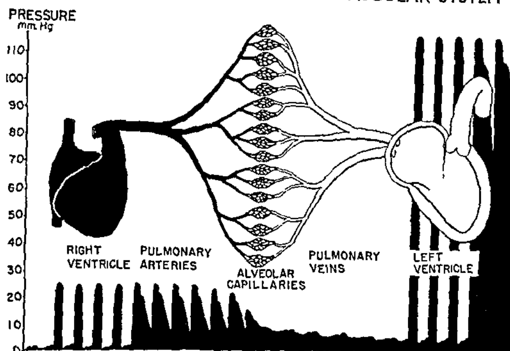


FIGURE 2 Since the pulmonary arterial system offers slight resistance to blood flow, the pressure difference between pulmonary artery and left atrium amounts to only 4 to 6 mm Hg This low pressure head drives the same volume of blood through the pulmonary circuit as flows through the systemic circulation with a gradient of some 90 mm Hg

eter consist essentially of poorly supported endothelial tubes which abruptly break up into a profusely anastomotic capillary network Thus, there are no vessels corresponding to the muscular arterioles in the systemic circulation The alveolar capillaries are the principal structural element in the walls of the respiratory membranes (Fig 1) The capillary network is so dense that in many alveoli the space between capillaries is less than their diameter [2]

BLOOD FLOW THROUGH THE PULMONARY CIRCULATION

Resistance to Blood Flow through the Pulmonary Circuit

For several reasons the normal intravascular pressures do not fall abruptly in the small vessels of the lung (Fig 2) (*a*) There are no high-resistance muscular arterioles in the terminal ramifications of the vascular tree (*b*) The pulmonary capillaries are extremely voluminous, diffusely anastomotic and of relatively large caliber (*c*) The pulmonary vessels are passively distended in response to increased pulmonary blood flow (*d*) There is a large reserve capacity in the lung which is not fully utilized except under conditions of stress For example, an entire lung with all its capillary bed can be removed without increasing the pulmonary arterial pressure (*e*) Finally, all vessels in the pulmonary vascular tree have a somewhat larger caliber than corresponding vessels in the systemic circulation The net effect is a total peripheral resistance to flow only about one-fifteenth of that in the systemic circulation

Pressures in the Pulmonary Circulation (Fig 2)

During systole, the right ventricular pressure rises to about 22 mm Hg The pulmonary arterial pressures average about 22/8 mm Hg with a mean arterial pressure of about 13 mm Hg [3] The pressure at the point of outflow from the pulmonary circuit (the left ventricular diastolic pressure) is about 7 mm Hg (Fig 2) Thus, a pressure gradient of only about 6 mm Hg will force through the pulmonary circuit the same quantity of

blood which passes through the systemic circuit under a gradient of 90 mm Hg Furthermore the pulmonary arterial pressure may remain unchanged or diminish slightly when the cardiac output increases threefold One case has been described in which a pressure gradient of 4 mm Hg propelled 15 liters of blood per minute throu h the pulmonary circuit[4] The small pressure gradient between the pulmonary artery and the left atrium is the basis for the statement that the pulmonary circuit has an exceedingly slight resistance to flow

Vasomotor Effects on Pulmonary Resistance

It is generally believed that the changes in pulmonary resistance associated with increased pulmonary blood flow are largely or entirely due to passive distention of these vessels[5] Evidence demonstrating active vasomotor responses in the lungs has been quite unimpressive However pulmonary arterial hypertension is frequently associated with congenital and rheumatic valvular heart disease and may be greatly alleviated by appropriate therapy (*vide infra*) Such evidence indicates that active vasoconstriction in the pulmonary arterial system contributes to the increased pulmonary resistance[6 7] Inhalation of gases with low oxygen tension produces increased resistance to blood flow If the low oxygen tension is confined to one lung blood flow through this region is diminished diverting blood into the unaffected region[8 10] If the observation that no arterioles exist in the pulmonary vascular tree is anatomically correct, changes in pulmonary resistance are accomplished by variations in caliber of the arterial branches which are well supplied with innervated smooth muscle

FUNCTIONS OF THE PULMONARY CIRCULATION

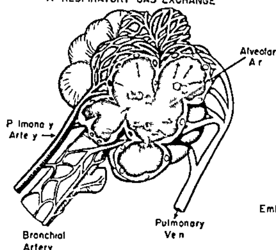
The pulmonary circuit simultaneously performs three functions (*a*) gaseous exchange of oxygen and carbon dioxide between the alveolar air and blood (*b*) storage of blood in a variable volume reservoir and (*c*) blockade of foreign particles, thrombi and other types of emboli circulating in the systemic venous blood

Gas Exchange The Principal Function of the Lungs

Blood passing through the alveolar capillaries of the lungs is effectively spread into a layer about 10μ thick and 100 sq M in area The alveolar air is separated from the blood by only two layers of tissue, the endothelial cells and a delicate alveolar membrane Some investigators deny the existence of an alveolar membrane between the endothelial barrier and the alveolar spaces The oxygen tension is lower and the carbon dioxide tension is greater in blood entering the alveolar capillaries than in the alveolar air Blood traverses the alveolar capillaries in about 1 second Propelled by their diffusion gradients oxygen and carbon dioxide are exchanged so rapidly that blood leaving the alveolar capillaries is *normally in virtual* equilibrium with the alveolar *air (Fig 3 4)* The action of carbonic anhydrase in the erythrocytes and rapid dissociation of carbon dioxide from reduced hemoglobin as it is converted to oxyhemoglobin facilitate exchange of carbon dioxide The gaseous exchange is sufficiently rapid only when the *diffusion distances* are extremely small Thus very thin layers of fluid accumulating between the alveolar air and the blood can seriously retard respiratory exchange

Oxygen and carbon dioxide cannot be exchanged when the blood flows through collapsed alveoli because it does not come in contact with alveolar air Thus blood passing through non aerated alveoli would *retain* the character of venous blood However, resistance to flow increases markedly in atelectatic lung tissue automatically shunting blood from non aerated portions into the inflated regions of the lung Collapse of pulmonary tissue is believed to reduce the distention of the vessels increasing the resistance to flow Diminished partial pressure of oxygen in the alveoli also tends to increase

FUNCTIONS OF THE LUNGS



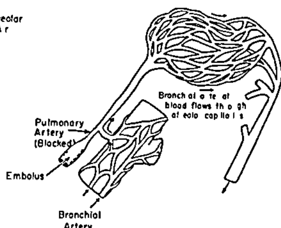


FIGURE 3 *A* Gas exchange the principal function of the lungs occurs because of the higher concentration of oxygen and lower concentration of carbon dioxide in the alveolar air than in the venous blood arriving at the pulmonary capillaries

B Embolic obstruction of pulmonary arteries does not produce necrosis of pulmonary parenchyma because bronchial arterial blood is diverted through dilated channels into the alveolar capillaries Because of this dual blood supply the lungs can serve as filters for emboli without self-destruction

pulmonary resistance, as noted above At the end of a normal inspiration, the lungs are not completely inflated since an additional 2 liters of air can be inspired A considerable proportion of the lung must be only partially inflated Blood flowing through these regions is either stagnant or slowly moving and contributes little to the circulation of the body as a whole In one sense such tissue is a reservoir of blood

Reservoir Function of the Lungs

Since the pulmonary vessels constitute a low-pressure, distensible system, any slight increase in outflow pressure at the left ventricle or relative increase in input from the right ventricle will cause considerable quantities of blood to accumulate within the lungs Presumably, engorgement of the lungs will cause elevated pressure throughout the pulmonary circuit because the pressure gradient is so shallow However, it seems likely that considerable distention may occur with little elevation in pressure For example there is evidence that considerable quantities of blood are displaced into the heart and lungs after reclining [11, 12] In summarizing such data, Sjostrand[13] pointed out that an average of more than 600 ml of blood was shifted from the lower extremities to the rest of the body after five standing subjects assumed the reclining position Seventy-eight per cent of this blood was taken up in the thorax, three-quarters of which was accommodated in the lungs Another 20 per cent was apparently distributed in the head, neck arms, shoulders and hip region, while only 2 5 per cent accumulated in the abdomen On this basis, the blood which distends vessels in dependent extremities is shifted from many other regions but principally from the lungs According to these studies the splanchnic bed supplies only about 2 5 per cent of the blood for this particular adjustment As much as 25 per cent of the blood in the thorax (heart and lungs) may be shifted to the legs This reserve volume in the pulmonary circuit appears to be distributed diffusely through the lungs where it is held "on tap" until drawn from in order to effect the rapid readjustment of the circulation required for larger cardiac output Reserve blood in the lungs has been compared with water dammed up behind a sluice gate where it compen-

sites for occasional variations in supply and output On this basis the lungs have an important reservoir function This distensible vascular network may also serve to cushion transient difference in right and left ventricular output e g at the onset of violent exercise

Filter Action of the Lungs

If foreign bodies thrombi air bubbles or fat particles enter the systemic arterial system, they generally occlude a terminal artery within some organ This reduces or eliminates circulation to the tissues supplied by that arterial branch and the tissue cells frequently die If it occurs in a vital organ such as the brain or heart this is a serious event. Fortunately most of the emboli enter the blood stream on the venous side of the circulation and lodge in the lungs By virtue of a double circulation the pulmonary vascular tree is particularly adapted to filtering out these circulating vascular plugs without self-destruction

In parallel with the pulmonary arterial system the bronchial arteries transmit oxygenated blood throughout the walls of the bronchial tree as far peripherally as the bronchioles[2] Anastomotic connections between pulmonary and bronchial arteries are not believed to occur normally[14] However anastomoses of small caliber exist in the walls of the bronchioles and alveolar ducts where they share common capillary beds (Fig 3B) The venous drainage from the bronchial arterial system is by way of the pulmonary vein except in the first two or three divisions of the bronchial tree Obstruction or occlusion of a branch of the pulmonary artery does not affect the blood supply to the bronchial system[15] Dilatation of channels in the common capillary networks provides a mechanism for diverting oxygenated blood through th alveolar membranes when pulmonary arterial flow is arrested or reduced (Fig 3B) Thus lung tissue is rarely destroyed by obstruction of the pulmonary blood supply The diffuse anastomatic connections between adjacent alveoli provide additional protection against occlusion of small peripheral branches of the pulmonary arterial system The affected lung tissue survives while the embolus is resorbed or recanalized, after which the tissue resumes its activity There is every reason to believe that this sequence of events occurs repeatedly during any person s lifetime without producing symptoms unless the embolus is very large or is located in a critical position

Elevation of pulmonary venous pressure simultaneously raises the pressure in both the alveolar and the bronchial capillaries This phenomenon may represent an anatomic basis for the bronchial edema which is often associated with pulmonary congestion and edema (Chapter 9)

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Part Two

REGULATION OF THE CARDIOVASCULAR SYSTEM

Introduction to Part Two

A fundamental characteristic of the cardiovascular system is the prompt, integrated adjustments in the function of the peripheral vessels and of the heart in response to varying demands of various tissues for greater or lesser flow of blood The principles of peripheral vascular control are considered first (Chapter 5) because the load of the ventricles is dictated by conditions in the peripheral vascular bed, under the influence of multiple controlling mechanisms In Chapter 6 the regulation of the cardiac output is considered in relation to mechanisms by which the heart and peripheral circulation are integrated to work in harmony The results of recent investigations are presented to indicate the complexity of cardiac regulation, including evidence indicating the prominent role of neural and hormonal controls in this process Chapter 7 is devoted largely to a consideration of mechanisms by which the stroke volume of the ventricles could be directly affected by neural and hormonal mechanisms which influence the "physiologic state" of the myocardium Certain physical and architectural properties of the ventricular chambers are reviewed because they unquestionably affect the filling and emptying of the ventricular chambers

Principles of Peripheral Vascular Control

The cardiac output is not directly regulated by the heart Instead the blood flow through various tissues is adjusted in relation to their functional requirements by complex controlling mechanisms The left ventricle normally adjusts rapidly and precisely to changes in peripheral resistance and blood flow in the entire systemic circulation The right ventricular output must also be adjusted to precisely balance the flow through the systemic circulation In this sense the heart plays a relatively passive role in the regulation of its own output although its failure to respond adequately to the needs of the body results in clinical signs and symptoms referable to the heart and circulation It is easy to become so engrossed with the noises and electrical activity originating from the heart as to disregard the principal function of the circulatory system namely the maintenance of a relatively constant and favorable environment for the cells of the body

THE FUNDAMENTAL REQUIREMENTS OF PERIPHERAL VASCULAR CONTROL

The human body is comprised of billions of cells variously specialized grouped and organized to perform many different functions Unlike self sufficient unicellular organisms which draw their sustenance from a relatively large expanse of surrounding water body cells exist within a relatively confined space They can survive and function only so long as their immediate environment contains an adequate supply of the essential nutrient materials and a limited concentration of waste products In other words the temperature pH and concentration of various constituents must be maintained within certain limits A living cell continuously utilizes certain types of molecules (oxygen glucose amino acids etc) As these substances are depleted in the immediate environment of the cell other molecules of the same substances move toward this region of reduced concentration in response to a diffusion gradient The rate of diffusion is determined by the concentration gradient and the distance between the blood and the cells (Fig 1) Cells which consume essential materials at a rapid rate must either be situated near capillaries or operate effectively at low concentrations of the various vital materials Thus tissues with high metabolic rates (brain muscle kidney etc) characteristically have dense capillary networks through which blood flows at rapid rates By this mechanism high concentrations of essential substances are maintained near the capillary walls providing a steep gradient for diffusion Cells with lower requirements are dispersed farther from the capillaries and are less affected by cessation of blood flow Elimination of waste products proceeds in the reverse direction propelled by diffusion gradients with maximum concentrations at the site of production in the cells Thus the delivery of substances to the tissues involves two steps transportation by the blood to the capillary beds and local delivery by diffusion The efficiency of the circulatory apparatus depends upon the success with which it provides adequate diffusion gradients within the tissues

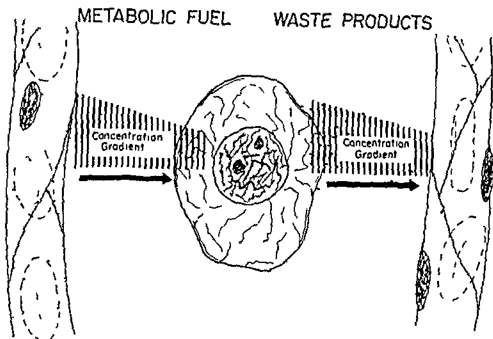


FIGURE 1 Metabolic fuels and waste products are transferred between the blood and tissue cells by diffusion The rate of transfer depends upon the concentration gradient for each substance and the distance of diffusion

OXYGEN EXTRACTION IN ACTIVE AND INACTIVE TISSUES

ARTERIAL O_2 VOL %
INACTIVE TISSUES
VENOUS O_2 VOL %
20 15 10 5 0

ARTERIAL O_2 VOL %
ACTIVE SKELETAL MUSCLE
VENOUS O_2 VOL %
20 15 10 5 0

FIGURE 2 The quantity of oxygen extracted from the blood *during its flow through capillaries is* determined by the relationship between the rate of oxygen utilization and the blood flow

A *Slight* oxygen extraction and small arteriovenous oxygen differences occur in tissues with relatively small oxygen requirements *and active blood flow* e g skin

B, Tissues which *release energy* at rapid rates, e g contracting muscle extract a major portion of the oxygen from the blood

The metabolic activities of certain tissues may vary widely with corresponding variations in their use of different substances The maximal effort sustained by a tissue depends upon the available supply of vital substances Generally the most crucial substance is oxygen, which is rapidly depleted because only limited quantities are stored in the body Arterial blood entering capillary networks normally contains about 19 cc of oxygen per 100 cc Oxygen utilization in relation to blood flow determines the quantity of oxygen remaining in the venous blood (Fig 2) In some tissues e g skin, kidney and connective tissue the blood flow is high whereas oxygen extraction is relatively slight only 1 or 2 cc of oxygen may be removed from each 100 cc of blood Active skeletal muscle and myocardium extract as much as 70 per cent or more leaving little oxygen in the venous blood Thus, the difference in the oxygen contents of arterial and venous blood (A-V oxygen difference) varies widely from tissue to tissue (Fig 3) The average A-V oxygen difference, using mixed venous blood, ranges around 4 to 6 cc per 100 cc of blood

If the metabolic activity of a tissue suddenly increased without a change in blood flow, the concentration of oxygen in and around the cells would drop the diffusion gradient would steepen, the rate of diffusion would accelerate and the A-V oxygen difference would widen On the other hand if an increased blood flow completely compensated for the increased oxygen utilization oxygen delivery would be increased without a change in A-V oxygen difference and with little drop in tissue oxygen tension Circulatory adjustment to varying metabolic de-

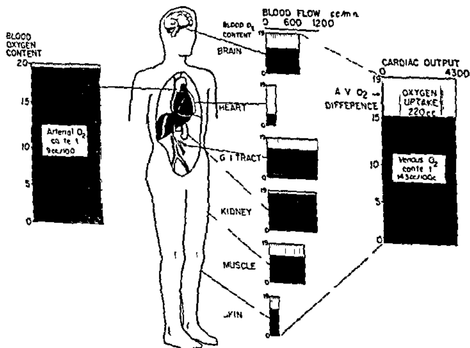


FIGURE 3 The blood flow through some tissues is voluminous in relation to the oxygen requirements (kidney and skin) In contrast the myocardium and contracting skeletal muscle extract most of the oxygen from the blood The arteriovenous oxygen differences represent the relationship between blood flow and oxygen utilization in various tissues

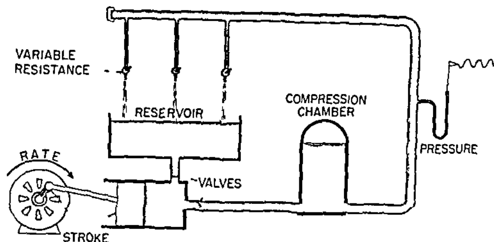


FIGURE 4 The principles of cardiovascular control can be illustrated by a simple hydraulic model In this system the pressure head is determined primarily by the relation between the resistance to outflow and the pump output (stroke volume × stroke rate) To maintain the pressure at a constant level any change in outflow resistance must be promptly compensated by an adjustment in the pump output The pressure head outflow resistance and pump output are so intimately related that none can be altered without affecting the others

mands is directed toward maintaining diffusion gradients, but is rarely sufficiently precise to prevent a reduced oxygen content of venous blood or an increased A-V difference in blood flowing through the active tissue

Obviously, the blood flow through certain specialized organs is not dictated solely by the metabolic demands of their component cells For example the blood flow in the skin and kidneys greatly exceeds that required to deliver oxygen to the cells because the specialized functions of these organs (*temperature regulation and urinary excretion*) require a voluminous blood flow beyond their oxygen requirements Thus, circulatory adjustments must be made to sustain both the survival and the specialized functions of various organs performing diversified roles in the total body economy

Adaptability of the blood flow is attained by the integration of the available volume flow in relation to the individual requirements of various organs and tissues (vasomotor control) and by changes in the total blood flow through the system (cardiac output) Let us now consider the principles of cardiovascular control by which the circulatory system adapts to the changing requirements of the various tissues

THE BASIC CONCEPTS OF CARDIOVASCULAR CONTROL

The fundamental requirements for regulation of cardiac output can be conveniently described in terms of simple hydraulic *pumping systems A common type consists* of a large tank supported at sufficient height to give a head of pressure In such a system the pump can be set to operate at constant speed variations in demand being accommodated at the expense of the reserve volume in the tank However this type of *system could not easily* be adapted to man or animals because a large quantity of blood would have to be carried around above the head Portability can be achieved only if the capacious storage tank is replaced by a small pressure tank However in this case an increase in outflow from the system must be rapidly and precisely compensated by adjusting the output of the pump Consider a model circulation consisting of a pump a compression chamber and several variable orifices (Fig 4) By adjusting stroke volume stroke frequency and total outflow resistance, the mean pressure in the system can be maintained at *constant levels for indefinite* periods of time If the stroke frequency and outflow resistance are properly set the pres-

sure in the system never drops to zero between strokes Once such an equilibrium is established alterations in any one of the three variables will be immediately reflected by changes in pressure within the system To maintain a constant pressure any alteration in one variable must be simultaneously balanced by adjustments in the others so that inflow always equals outflow For example if the stroke frequency is increased and the outflow resistance is not changed, the stroke volume must be reduced until pump output is restored to previous levels Similarly opening one outflow orifice more widely would produce a fall in pressure unless the resistance to outflow from other valves was increased or the pump output was rapidly augmented by either increased stroke volume or stroke frequency In this system maintenance of a constant mean pressure automatically provides a precise balance between inflow and outflow This schematic model illustrates the fundamental principle by which the cardiac output is continuously adjusted to compensate for changes in peripheral resistance The mean arterial blood pressure tends to stay within a relatively narrow range both at rest and during activity To the extent that requirements of the tissues for blood flow are reflected by their changes in peripheral resistance cardiac output is continuously adjusted to equal the total blood flow in all the tissues

FUNCTIONAL ANATOMY OF PERIPHERAL VASCULAR CONTROL

Zweifach[1] has described two distinct types of capillaries arteriovenous capillaries and true capillaries The A V capillaries are thoroughfare channels which follow fairly direct courses from arterioles to venules In general blood flows continuously through the A V capillaries the rate of flow being varied through changes in the caliber of the muscular arterioles and of the A V capillaries themselves A V capillaries are invested with smooth muscle which is abundant at the arteriolar end and more diffusely distributed toward the venular regions (Fig 5) Branching from the A V capillaries are the 'true' capillaries which are intricately joined to form complex networks lying between adjacent thoroughfare channels The true capillaries have no smooth muscle except for muscular cuffs (precapillary sphincters) at their points of origin from the A V capillaries Capillaries from the vascular network rejoin the A-V capillaries near the venular end but no smooth muscle sphincters appear at these junctions If all the precapillary sphincters serving a capillary bed closed simultaneously blood flow through these channels would cease However at any one instant some precapillary sphincters are open while others are closed At intervals of 0 5 to 3 minutes some sphincters close and others open The caliber of the A V channels also fluctuates asynchronously Dilatation and constriction of the A-V capillaries and the different combinations of dilated precapillary sphincters produce a continuously changing pattern of flow through the capillary networks In a

VASOMOTION IN A CAPILLARY NETWORK

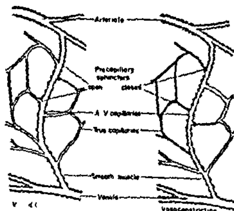


FIGURE 5 Capillary networks in some tissues at least, consist of arteriovenous capillaries (thoroughfare channels) and "true" capillaries The blood flow through the different portions of the capillary bed is affected by contraction and relaxation of smooth muscle in the arterioles A V capillaries and precapillary sphincters Phasic changes in the caliber in these regions produce cyclic alterations in the amount and distribution of blood flow through the various true capillaries (vasomotion)

particular segment of the capillary bed, the blood may flow rapidly through one channel for a period of time, then cease or even flow in the opposite direction depending on which sphincters are open The phasic changes in the caliber of the arterioles, A-V capillaries and precapillary sphincters have been termed "*vasomotion*" (Fig 5) *The rate of* blood flow through the individual channels is an expression of a gradient in capillary pressure *Blood flow* is rapid when capillary pressure in the arteriolar end of an A-V capillary is high in relation to venular pressure When flow ceases, the pressure throughout the capillary approximates that in the venules

The functional significance of vasomotion is being intensively investigated, particularly *in relation to abnormal vascular states, e g ,* shock It is apparent that this aspect of vascular control also has important implica*tions for normal function as well For ex*ample, phasic vasomotor activity is expressed in periodic changes in the volume of the finger[2] and fluctuations in arterial blood pressure It implies a more precise regulation of capillary blood flow in response to local tissue demands than could result if control were limited to the arterioles At the same time, descriptions of capillary blood pressure become more complicated because the pressure levels and gradients are continuously changing However, certain generalizations can be made If the pressure in the venules remains constant, vasomotion would affect *only the pressure gradients from arterioles* to venules When the arterioles, A-V capillaries and precapillary sphincters are dilated, the pressure gradients *along the channels are* steep and blood flow is rapid When the caliber of these channels is reduced by constriction, more of the potential energy is lost as friction before the blood reaches the capillaries The pressure at the arteriolar end of the capillaries is lowered, the pressure gradients become shallow or are eliminated and blood flow diminishes or ceases Total blood flow through a tissue is increased by prolonging the intervals of vasodilatation and reducing the periods of vasoconstriction The organization of capillaries illustrated in Figure 5 is believed to occur in those tissues which have widely varying levels of activity Vasomotion, as a *characteristic pattern of* peripheral circulatory control, has been observed in a number of tissues including rat *mesentery, bat wing* and subcutaneous connective tissues It is now being studied in other more important tissues[3]

Local Control of Capillary Flow

Metabolic demands of the tissues are met by controlling influences which appear to adjust blood flow through individual capillary networks as the functional requirements of the tissues vary An increase in carbon dioxide usually associated with reduc*tions in the oxygen tension and pH of the* tissues is believed to affect directly the local capillary networks producing vasodilatation *Although most experimental evidence for* this hypothesis is indirect, it is accepted largely because these changes are intimately related to the level of tissue activity and therefore are a logical influence on blood flow This regulatory mechanism would be particularly useful in tissues such as skeletal muscle, where blood flow is related primarily to metabolic rate During exercise more oxygen is used and more carbon dioxide and acids are produced However, the amount of oxygen extracted from blood is far greater in exercising than in relaxed muscles (see Figs 2, 3), indicating that blood *flow does not increase enough to compensate* for the increased demand

In tissues such as the skin and kidney, *where blood flow requirements are greatly in* excess of metabolic requirements, tension of oxygen and carbon dioxide cannot be a primary *factor in the control of blood flow* Cutaneous vessels are subject to a wide variety of neural influences from both local *reflexes and higher levels in the central* nervous system (temperature regulation emotional flushing) They are also affected by many chemical substances mechanical stimulation (stroking) and radiation (ultra-

violet infra red and roentgen rays) For the present discussion it seems desirable to distinguish between metabolic and functional controlling factors Metabolic controls alter the blood flow and cardiac output to meet oxygen requirements in tissues so that cardiac output is related to the total oxygen requirements of the body, i e, during physical exercise Functional controls produce changes in peripheral blood flow and cardiac output in relation to specialized activity such as the formation of urine or temperature regulation The higher levels of the central nervous system may produce cardiovascular adjustments which seem inappropriate to the situation i e blushing Emotional disturbances produce cardiovascular responses during anxiety or apprehension which would be suitable for increased physical exertion. In considering the mechanisms by which diverse signals from many areas provide an integrated cardiovascular control it is convenient to begin with the autonomic control of peripheral vessels

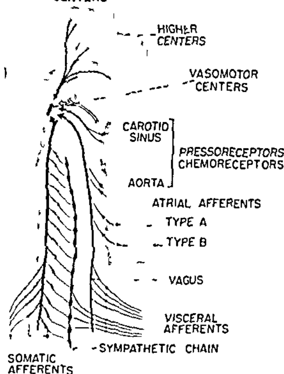
Autonomic Control of Peripheral Resistance

The sympathetic division of the autonomic system plays an important role in adjusting the peripheral vascular resistance The smooth muscle investing the arterioles A-V capillaries and precapillary sphincters is directly innervated by sympathetic nerve fibers Stimulation of the splanchnic nerves elicits a prompt elevation in systemic arterial pressure The preganglionic fibers which mediate this response originate in the intermediolateral cell columns of the spinal cord A transection of the spinal cord in the cervical region induces a marked reduction in arterial blood pressure which indicates that discharge of the sympathetic vasomotor fibers is strongly influenced by connections from above Section of the brain stem above the medulla oblongata does not produce such a fall in blood pressure This type of evidence indicates that somewhere in the medullary region is a center which more or less dominates the vasomotor outflow from the sympathetic nervous system Electrical stimulation of certain areas in the floor of the fourth ventricle produces a prompt rise in systemic arterial pressure Stimulation of adjacent areas produces a sharp reduction in arterial blood pressure These areas are termed 'vasoconstrictor and vasodilator' centers, respectively Anatomically, these centers are poorly defined, but functionally they appear to represent a source of nerve impulses which play upon the preganglionic cells of the intermediolateral cell column to influence the sympathetic discharge to the peripheral vascular networks and adjust the peripheral resistance and blood flow

A generalized sympathetic discharge also initiates the release of epinephrine which circulates through the blood and reinforces the direct sympathetic effects on the peripheral vasculature An elevation of arterial blood pressure is generally attributed to a generalized sympathetic discharge accompanied by a release of epinephrine However this does not necessarily mean that peripheral resistance is raised in all vascular beds in the body Indeed factors which characteristically induce vasoconstriction of the splanchnic bed frequently produce dilatation in skeletal muscle (as in fainting)[4, 5] and vice versa Both sympathetic nerve discharge and epinephrine tend to produce vasodilatation in skeletal muscles[6] On this basis it is unwise to speak of a generalized vasoconstrictor effect without proper reservations This subject is quite complicated and will not be considered in detail because it is not strictly pertinent to a consideration of heart disease For additional details and recent developments, the reader is referred to an excellent review by Barcroft and Swan[7]

The vasomotor centers with their efferent outflow down the spinal cord and out through the sympathetic system constitute a common pathway for vasomotor control (Fig 6B) The efferent discharge along this pathway is continuously influenced by nervous impulses from many different sources converging upon the vasomotor centers For example hypothalamic temperature regulating

NEURAL MECHANISMS FOR PERIPHERAL VASCULAR CONTROL



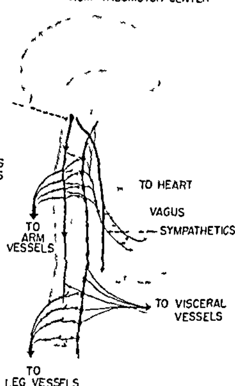


FIGURE 6 *A* The vasomotor centers in the medulla receive afferent impulses originating from many different areas in the body including the higher centers of the nervous system pressoreceptors from the heart and great vessels afferent nerves from the viscera and somatic pain afferents
B Impulses discharged from the vasomotor centers descend the spinal cord and influence cell bodies in the intermediolateral cell column which in turn initiate sympathetic nerve impulses conducted to the blood vessels in all parts of the body

centers act through the vasomotor centers to alter blood flow in the skin and thus to maintain body temperature by controlling heat loss The emotional content of thought can induce vasodilatation in the skin (flushing) or such extensive peripheral vasodilatation that arterial pressure falls precipitously (emotional fainting) Anticipation of impending exertion produces increased peripheral blood flow and elevated cardiac output even before increased oxygen delivery is required Blood flow through the splanchnic bed is diminished during exercise and increased during active digestion Some of the sources of afferent nerves which play upon the vasomotor centers are illustrated schematically in Figure 6 *A* According to Wall and Davis,[8] afferent impulses arise from higher centers in many different regions of the brain, including the sensory-motor cortex, posterior orbital-anterior insular system and the temporal-cingulate system in addition to the hypothalamus [9] The specific functional significance of these systems has not been elucidated with relation to over-all autonomic control Functional evidence of autonomic influences originating from higher centers is implicit in many everyday experiences

Pressoreceptors in the carotid sinus and aortic arch respond to changes in arterial blood pressure, giving rise to corresponding volleys of nerve impulses which bombard the vasomotor centers (Fig 7) Impulses recorded from the central end of a cut splanchnic nerve arrive with cyclic variations in frequency in time with the arterial pulse wave The discharge reaches greatest frequency during the peak of arterial pressure but this coincidence is probably due to delays in neural transmission since marked

and sustained increases in frequency are induced by reduction in mean arterial pressure[10] This bombardment of nerve impulses presumably exerts a vasomotor effect on the splanchnic bed under normal conditions Although it is difficult to demonstrate similar discharges along sympathetic fibers to other regions they probably occur

Chemoreceptors also located in the vicinity of the carotid sinus and aortic arch are affected by changes in the chemical composition of the arterial blood When the carotid sinus region is isolated from the circulation and perfused with solutions having low oxygen tension low *p*H or increased carbon dioxide concentrations, an elevation in systemic arterial pressure is produced The vasomotor centers are also directly affected by the oxygen and carbon dioxide tensions of the blood perfusing the central nervous system

In the past reflexes originating in the heart and great veins have been postulated by Bainbridge[11] and McDowall[12] Although the particular vascular responses upon which these concepts were based have not been universally confirmed[13 14] there has been a growth of interest in afferent impulses traveling along fibers in the vagal trunk which display cyclic variations in frequency in time with the cardiac cycle[13 17] Paintal[18] divided fibers originating from the atria into two groups type A which discharge during atrial systole and type B which discharge during atrial diastole (Fig 7*B*) Since these receptors apparently respond to stretch and are located on the low pressure side of the circulation Sieker Gauer and Henry[19] believe that they may actually monitor blood volume as it affects the distention of central veins and atria This hypothesis has been supported by evidence that artificially increased distention of the intra thoracic vasculature augments urine flow The importance of such a mechanism will be considered further in relation to the control

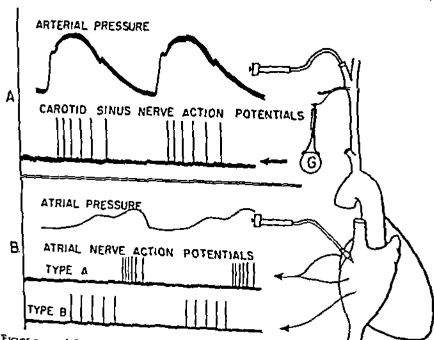


FIGURE 7 *A* Individual stretch receptors in the carotid sinus discharge impulses at a frequency dependent primarily upon the arterial pressure (after Bronk and Stella[22]) *B* Stretch receptors from the atria have been divided into two groups type A which discharge during atrial systole and type B which discharge during atrial diastole (after Paintal[18])

of blood volume (see Chapter 9) These afferent nerves may also play a role in the regulation of central venous pressure (see Chapter 3)

Visceral afferent fibers enter the vagus and sympathetic trunks from many other sources, i e, pain endings, chemoreceptors,[15] pacinian corpuscles,[20] etc The profound diminution of systemic arterial pressure produced by stimulating arteries,[21] veins, deep tissues and internal organs indicates that they may exert powerful influences on the vasomotor center Somatic afferent fibers (e g, pain) reflexly elevate the systemic arterial blood pressure, presumably through the vasomotor center Clearly, the rate and distribution of discharges along the sympathetic outflow to the peripheral vascular system are continuously influenced by the interplay of a wide variety of afferent nerves which directly or indirectly converge upon the vasomotor centers

Regulation of Systemic Arterial Blood Pressure

In view of the tremendous number of pathways along which nervous impulses reach the vasomotor centers, some stabilizing mechanism must exert an over-all control to prevent circulatory disorganization when several major areas of the body simultaneously require increased blood flow For example, running at full speed on a hot day after a full meal would theoretically require increased blood flow through the muscles, skin and gastro-intestinal tract However, if all these vascular beds suddenly dilated, the arterial blood pressure would tend to drop precipitously and blood flow through other vital regions would be jeopardized Actually, splanchnic vasoconstriction is the typical reaction to this situation Referring to the schematic diagram in Figure 4, a monitoring system which maintains the pressure in the system by a control of peripheral resistance and output of the pump will automatically provide a balance between the inflow and outflow so that the capacity of the pump is not exceeded If the output of the pump cannot fully compensate for increased flow out of the system, the pressure monitoring system will shut down the flow in some of the outflow channels until balance is restored Pressoreceptors on the arterial side of the systemic circulation have the same role in the regulation of arterial blood pressure in spite of constantly shifting patterns of blood flow distribution to the various tissues of the body

Recording impulses from single stretch receptors in the carotid sinus, Bronk and Stella[22] found that a steady pressure produced a train of impulses which continued indefinitely at a frequency slightly less than the initial value A drop in pressure produced a transient but complete cessation of impulses from the end organ After a few seconds, the discharges recurred at a frequency characteristic of the new pressure level According to Landgren[23] these baroreceptors respond to a pressure rise by an increased frequency of discharge within a certain pressure range This "recording range of the receptor" varies in different end organs, extending from 30 to 200 mm Hg The threshold pressure of a steady discharge varied between 80 and 120 mm Hg A minimum impulse discharge has been obtained between 50 and 60 mm Hg during pressure reduction to 0 mm Hg Below the minimum discharge rate the impulse frequency increased, possibly because of deformations of the arterial wall at these low pressures

Heymans et al [24 25] emphasized that the arterial pressure stimulates the pressoreceptors through stretching of the arterial wall the degree of which is determined by the arterial pressure and the distensibility of the wall They have demonstrated that, after topical application of various drugs the state of contraction and resistance to stretch of the arterial wall are primary factors affecting these receptors These observations indicate that the response of the baroreceptors may be independent of the arterial pressure through changes in distensibility (see also Fig 7, Chapter 2)

SUMMARY INTEGRATION OF PERIPHERAL VASCULAR CONTROL

Four levels of peripheral vascular control can be described (a) mechanisms for initiating a change in blood flow (b) compensatory mechanisms for maintaining the vascular pressures within a tolerable range (c) ancillary mechanisms which come into play when the cardiovascular-pulmonary adaptations are insufficient for the oxygen requirements and (d) mechanisms which promote sustained elevation of systemic arterial blood pressure as in essential hypertension

Initiating Mechanisms

Presumably vasodilatation in the active regions is the first event in altering the flow pattern to meet increased demands for blood flow through specific capillary beds In some situations the higher centers of the central nervous system initiate peripheral vasodilatation e g blushing or fainting temperature regulation or anticipation of physical exertion Actual contraction of skeletal muscle involves impulses passing down motor nerves from cerebral cortex Pyramidal tract fibers may send collaterals to the medulla and pons[26] which may influence the vasoconstriction center [7] When the increased peripheral blood flow is needed to meet an increase in metabolic rate the increased utilization of oxygen and the faster production of carbon dioxide and other acidifying substances directly induce predominant vasodilatation e g during contraction of skeletal muscle Under some conditions autonomic reflexes may be initiated by impulses along visceral and somatic afferent nerves to accelerate flow through particular regions Vasodilatation in the skin and gastro-intestinal tract may be affected by such reflex activity Regardless of the initiating mechanisms vasodilatation and diminished resistance to blood flow through any large portion of the circulatory bed tend to depress the systemic arterial blood pressure which immediately requires compensatory mechanisms

Compensatory Mechanisms

Very slight alterations in the systemic arterial blood pressure reduce the rate of firing of pressoreceptor end-organs in the carotid sinus aortic arch and elsewhere in the systemic arterial system These impulses play upon the medullary centers and influence both the degree of peripheral vasoconstriction and the output of the heart A drop in blood pressure affects the pressoreceptor discharge to the cardio-accelerator center which, in turn emits impulses to quicken heart rate and increase stroke volume This center may also be influenced by other mechanisms which are not yet clear (see Chapter 6) At the same time, a greater degree of vasoconstriction is induced in regions where the blood flow normally exceeds the functional demands Diminishing the blood flow through the kidney and splanchnic bed is particularly important in the vascular compensation to vigorous physical exercise Gammon and Bronk[20] demonstrated that pacinian corpuscles in the mesentery fire nerve impulses at rates related to the pressure in the mesenteric arteries and may continuously monitor the distention of the mesenteric vessels Although the reflex mechanism described by Bainbridge remains controversial [15] a great deal of interest has recently developed regarding the function of visceral afferent nerves originating in the walls of the heart Stimulated by the work of Jarisch [14] information is rapidly accumulating in this general area (*vide supra*)

From this abbreviated description it becomes plain that the pressoreceptor mechanisms are far more complex than had been previously believed However it seems clear that these compensatory reflexes act to maintain the arterial and venous pressure relations within limits in spite of large variations in the distribution and amount of peripheral blood flow In this way the blood flow through such vital organs as the brain and heart is not jeopardized by variations in the requirements of other tissues

Ancillary Mechanisms

In the vicinity of the carotid sinus and aortic arch are chemoreceptors which vary their rate of impulse discharge in response to changes in the partial pressure of oxygen and carbon dioxide and to variations in the *p*H A reduction in the oxygen and an increase in the carbon dioxide concentration and acidity of the blood flowing through these so-called "carotid and aortic bodies" ultimately result in a generalized increase in systemic arterial blood pressure Similarly, the vasomotor centers in the medulla are sensitive to altered oxygen and carbon dioxide tensions in their immediate environment In both cases, the blood which perfuses these tissues has been arterialized in passing through lungs The arterial blood normally has remarkably constant levels of oxygen, carbon dioxide and acidity even during exertion The chemoreceptor mechanisms would be called into play only when the cardiovascular-pulmonary system failed to meet the demands of the organism Just which vascular beds are subject to vasoconstriction as a result of chemoreceptor activity is not known, nor has the functional significance of these mechanisms in the normal individual been established In patients with pulmonary disease or congenital malformations of the heart with venous-arterial admixture, the chemoreceptor mechanisms may assume greater importance

* * * * *

This brief review of the mechanisms which influence peripheral vascular resistance and blood flow is necessarily superficial and incomplete This background material was included to stress the fact that the amount of work which the heart must accomplish is dictated largely by the conditions in the peripheral vascular system Many of the mechanisms which influence peripheral vascular responses also affect heart rate and, presumably, stroke volume as well

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Chapter 6

The Regulation of Cardiac Output

The fact that arterial blood pressure tends either to remain normal or to become slightly elevated when systemic blood flow is increased means that the compensatory mechanisms governing cardiac output are both rapid in their action and precise in their control. Referring back to the hydraulic model illustrated in Figure 4, Chapter 5, it is clear that lowered total peripheral resistance must be promptly countered by a corresponding increase in cardiac output or the arterial blood pressure will fall precipitously. Cardiac output is determined by the heart rate and the stroke volume, both of which must be integrated by appropriate regulatory mechanisms. In the normal individual, *cardiac output is increased by simultaneous* acceleration of the heart and by augmented stroke volume. However, for purposes of discussion they will be treated individually.

CONTROL OF HEART RATE

Normally the heart rate is determined by the frequency with which the S-A (sinoatrial) node generates impulses. As pointed out in Chapter 1, the autogenic rhythmicity of the S-A node is influenced by the action of sympathetic and parasympathetic nerves through the chemical substances they release —epinephrine-like substances and acetylcholine. The retarding effect of acetylcholine released by vagal discharge usually predominates in controlling heart rate. Through reciprocal innervation in the central nervous system, *acceleration of the heart often signifies* simultaneously decreased vagal discharge and increased sympathetic activity in nerves terminating at the S-A node. It is of interest to consider the ultimate sources of the impulses which influence the activity of the S-A node.

Distribution of Autonomic Fibers in the Heart

Nerve fibers from both the vagus and the sympathetic chain enter the cardiac plexuses where they become thoroughly intermingled (Fig. 1). It is impossible to trace the ana-

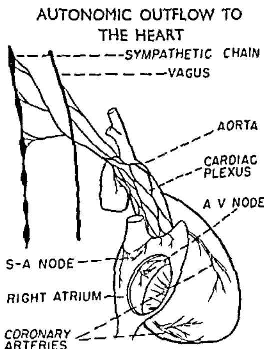


FIGURE 1. The sympathetic and parasympathetic outflow to the heart enters the cardiac plexus *and becomes thoroughly intermingled.* Judging from functional responses, the sympathetic fibers are distributed throughout the entire heart but are concentrated at the S-A and A-V nodes. Parasympathetic fibers converge on the S-A and A-V nodes but *are also distributed to the atrial musculature* and to the coronary vessels. Parasympathetic influences on the ventricular myocardium remain somewhat controversial.

tomic pathways of individual nerve fibers through this complex maze to their terminations in the heart and coronary vessels.

Sympathetic nerve fibers converge upon *the S-A and A-V (atrioventricular) nodes,* but are also widely distributed throughout the muscular walls of both the atria and the

ventricles. The epinephrine like substances released at these nerve endings act to quicken the heart rate and to increase myocardial irritability and contractility

Terminals from the vagi are also concentrated near the S-A and A V nodes and are widely distributed to the atria and to the bundle of His and its bundle branches. Although the ventricular walls are generally believed to be devoid of vagal fibers para sympathetic discharge plays an important role in regulating coronary flow (see Chapter 8). Acetylcholine secreted at vagus nerve endings produces coronary constriction and may diminish myocardial contractility as well as depressing pacemaker activity. Impulses descend the vagus and sympathetic nerves continuously exerting appropriate controlling influence on the heart. By variations in the vagal and sympathetic 'tone' the heart rate coronary blood flow and myocardial co tractility are adjusted to meet the requirements of the moment. These nerve impulses originate from medullary centers which anatomically and functionally parallel the centers for vasomotor control. Indeed the regulation of heart rate and of the peripheral vasculature is so similar that only a few changes in labels would be required to use the same schematic illustration (Fig 6 Chapter 5) for the two systems

Medullary Centers of Cardio-acceleration and Cardio-inhibition

Electrical stimulation on the floor of the fourth ventricle in the medulla oblongata reveals two poorly defined regions which strongly influence heart rate. Stimulation of one region the cardio-accelerator center produces faster heart rates. Stimulation of the adjacent region the cardio-inhibitor center produces slower rates. The cardio-inhibitor centers are in close anatomic relation to the motor nuclei of the vagus nerves

Sources of Afferent Nerves Converging on the Cardioregulatory Centers

The vagus and sympathetic nerves conduct impulses which result from a more or less continuous bombardment of the cardio-accelerator and cardio-inhibitor centers by afferent nerves from all over the body. The cardioregulatory centers are influenced by afferent fibers corresponding to those which play upon the vasomotor centers (Fig 6 Chapter 5)

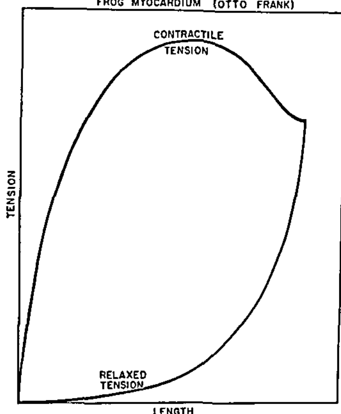
THE EFFECT OF HIGHER CENTERS ON HEART RATE. Impulses from the cerebral cortex impinge upon the cardio-accelerator and cardio-inhibitor centers as evidenced by many common experiences. Excitement anxiety fear and depression[1-4] affect the heart rate without any direct relation to metabolic activity. Cardio-acceleration occurs in anticipation of physical exertion before any significant increase in metabolism has occurred. An occasional individual can voluntarily alter his heart rate.[5] Clearly, the influence of higher centers on cardiovascular regulation cannot be ignored

PRESSORECEPTORS. Stretch receptors in the carotid sinus and aortic arch exert a powerful influence on the cardioregulatory centers. A change in arterial blood pressure is reflected in a corresponding change in the frequency of impulses from the baroceptors (Fig 7 Chapter 5) which in turn influences the cardioregulatory centers and the heart rate. A drop in arterial blood pressure induces an acceleration of the heart and vice versa

Digital pressure on a hypersensitive carotid sinus promptly produces bradycardia reduced peripheral resistance a severe drop in arterial blood pressure and syncope.[6] Insertion of a needle into the brachial artery of subjects in the erect position frequently produces a very similar response.[7] Such syncopal reactions termed vago-vagal reactions may be produced by a very wide variety of conditions.[8-10] Since sensory fibers from virtually all parts of the body influence heart rate and peripheral resistance only a few of the more prominent examples can be mentioned

VISCERAL AFFERENT FIBERS. Receptors in the walls of the atria and great veins (Fig 7 Chapter 5) have been implicated by Bain

FUNCTIONAL CHARACTERISTICS OF MYOCARDIUM



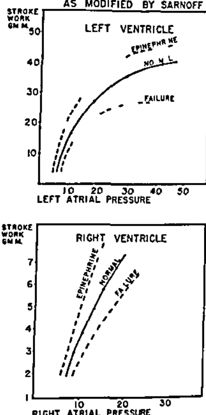


FIGURE 2 *A* The length tension curve of myocardial strips resembles that of skeletal muscle Progressive stretch of *relaxed myocardium is attended by a progressive increase in tension* The tension developed during contraction at varying degrees of initial stretch also tends to increase up to some critical level Over stretching of the myocardium produces a reduction in contractile tension (descending limb) although resting tension increases greatly

B The length tension relationship illustrated in *A* implies constant myocardial response to a specific set of conditions In controlled experiments on the intact heart Sarnoff and his associates[29] found that the relation between stroke work and filling pressure varied under different conditions producing a series of Starling curves Epinephrine improved the performance of the myocardium Interference with coronary blood supply (failure) depressed the myocardium and produced a descending limb at high filling pressures

bridge[11] in a reflex *tachycardia* produced by rapid infusion of saline Other investigators[12 13] have reported *bradycardia* from the same type of procedure as indicated in Chapter 5 Stimulation of internal organs may produce drastic cardiac inhibition For example, stimulation of nerve endings in the upper portion of the respiratory tract may produce intense vagal depression of the heart rate Thus, anesthetists must be extremely careful during intubation of the trachea because increased vagal activity may lead to cardiac standstill and death Inhalation of irritant gases may intensely affect the heart rate Phasic changes in heart rate (sinus arrhythmia) occur during normal respiratory cycles

The gastro-intestinal tract is supplied with afferent nerve fibers which travel along the vagus to the medulla Nausea and vomiting are commonly associated with slowing of the heart whether they are due to digital stimulation of the pharynx or to ingestion of toxic substances Visceral pain fibers are widely distributed and have a powerful slowing effect on heart rate Painful stimulation of skeletal muscles may produce a similar autonomic response Pressure on the eyeball

may produce a profound slowing of the heart through the oculocardiac reflex' In general visceral afferent nerves originating in nearly all tissues and organs except the skin produce bradycardia In contrast somatic pain from the skin generally produces tachycardia along with some increase in arterial blood pressure

Clearly there is much to be learned concerning the interplay of various factors integrating the responses of the cardiovascular system This is especially true of the factors which control the stroke volume

FACTORS AFFECTING STROKE VOLUME UNDER EXPERIMENTAL CONDITIONS

Elucidating the function and control of the heart requires two separate steps The first step consists of studying the response of hearts under rigidly controlled experimental conditions The functional potentialities of the heart can be determined by maintaining certain variables as constant as possible and producing alterations in one factor at a time The data obtained in such experiments indicate the heart's response to conditions imposed by the investigator Even the most brilliant investigator is a very poor substitute for the normal controlling mechanisms Ultimately it is necessary to determine that concepts derived from controlled experiments are applicable to intact unanesthetized experimental animals and to man by direct measurements of the significant variables *In other words it is necessary to know what* actually occurs in normal individuals as well as what *can* happen under experimental conditions Evidence will be presented *in a subsequent section* that the response of *the heart to* various conditions in intact animals and *in* man cannot always be predicted from the traditional concepts

Wiggers[14] recently reviewed the *historical* development of basic concepts of cardiac function and control In 1895 Otto Frank recorded isometric and isotonic contractions of frog myocardium and established *that* within limits myocardium resembles skeletal muscle in developing greater tension as the resting length is increased His results summarized in Figure 2 were confirmed for the tortoise ventricle by Kozawa[15] Patterson Piper and *Starling*[16] *used the heart* lung preparation (Fig 3) to study the influence on cardiac function of variations in venous inflow outflow resistance and heart rate

Ventricular Response to Increased Venous Inflow in the Heart Lung Preparation

In the heart lung preparation the quantity of blood entering the ventricles was increased by elevating the reservoir illustrated in Figure 3 Experimentally induced elevation in venous return resulted in a higher venous pressure a slight increase in arterial blood pressure and greater diastolic and systolic volumes of the ventricles (Fig 3) Records of this type have been interpreted as follows (*a*) When the reservoir is elevated the venous pressure rises and diastolic filling is increased (*b*) The myocardial fibers fail to eject as much blood as entered during diastole so an additional increment of blood remains within the ventricle (*c*) The succeeding diastolic filling is even greater but the volume ejected remains less than that which entered (*d*) The diastolic filling exceeds the systolic ejection until the ventricles become distended to a point where the energy release by the myocardium is sufficiently increased to bring the inflow and outflow into balance (*e*) The equilibrium between inflow and outflow is maintained with the ventricles at their new large diastolic and systolic size until the volume load *is reduced* (*f*) As the reservoir is lowered the energy *released* by the myocardium is excessive for the volume of inflow and the *quantity* ejected exceeds the volume which entered *For a few beats* outflow exceeds inflow *until the* systolic and diastolic ventricular volumes return to a lower level actually smaller than during the control period in Figure 3

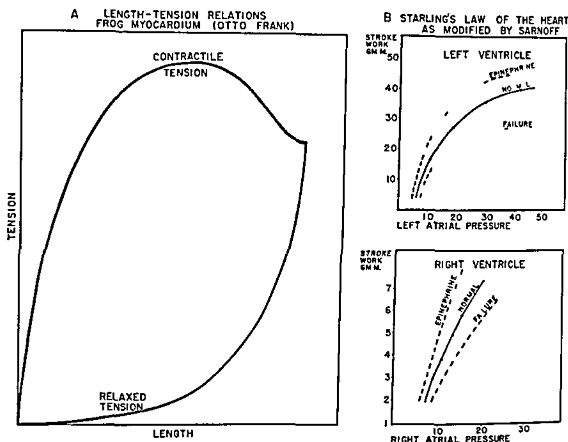


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normal output while operating at this larger size However if the ventricles become distended beyond some critical size the energy release becomes progressively less with further stretch on the myocardium and the heart fails The reduction of the contractile tension which occurs with excessive stretch in Frank s diagram (Fig 2) is a graphic illustration of this point Under these conditions increased diastolic distention with progressively higher venous pressure is attended by reduction in the contractile tension and in energy release This is the most common definition of heart failure

Wiggers and Katz[17] repeated these experiments using improved techniques Their results confirmed those of Starling and his associates that an increase in stroke volume was attended by an increase in diastolic volume (greater initial length of myocardial fibers) However they concluded that such changes were never dissociated from changes in initial intraventricular pressures Apparently, Starling was not convinced by this evidence because in subsequent publications he restated his belief that diastolic volume may change without corresponding alterations in filling pressure[18]

TRADITIONAL CONCEPTS OF VENTRICULAR CONTROL UNDER EXPERIMENTAL CONDITIONS

Variations in stroke volume are most frequently explained by a few fundamental rules which are generally held to apply so long as the functional condition of the myocardium remains within physiologic limits (*a*) The *cardiac output* is determined by the venous return (*b*) If the heart rate is constant the *stroke volume* is determined by the venous return (*c*) *Stroke volume* of the ventricles depends directly on the diastolic filling (*d*) The *tension* of resting myocardial fibers depends upon their length (Fig 2) (*e*) *Diastolic filling* (and diastolic volume) of the ventricles is determined by effective filling pressure (*f*) *The mechanical energy set free on passage from the resting to the contracted state depends on the length of the myocardial fibers* (*g*) The *tension* developed during contraction depends upon the initial length of the myocardial fibers (Fig 2)

A number of these concepts were derived from Starling's experiments and most of them have been erroneously cited at one time or another as "Starling's law of the heart" The concept that the diastolic volume is always determined by the effective filling pressure (*e* above) is contrary to both the results and the conclusions of Starling and his associates By the same token a constant relation between length and tension of resting myocardial fibers (*d* above) cannot be attributed to these investigators

Cardiovascular Response to Exertion Based on Traditional Concepts

Cardiovascular adaptation to physical stress is an appropriate example for consideration because exertional dyspnea is a very common symptom in patients with cardiac disease During exercise the cardiac output is closely related to the oxygen consumption The cardiovascular adjustments which provide a more rapid circulation of the blood in response to increased metabolic demands are usually described as follows As the skeletal muscles enter into phasic contraction their oxygen consumption is greatly increased the carbon dioxide production is accelerated and accumulation of metabolites produces an increase in H ion concentration All these factors act locally to produce dilatation of the arterioles The resistance to flow into these capillary networks is diminished and the blood flow through the active muscle is correspondingly increased The rapid outflow of blood from the arterial system through these widely dilated capillary networks tends to produce a drop in arterial blood pressure A fall in blood pressure reduces the discharge of arterial pressoreceptors promoting increased activity of the vasoconstrictor and the cardioregulatory centers Thus vasoconstriction in inactive tissues (e g renal and splanchnic vascular beds) may partly compensate for the vaso-

CARDIAC RESPONSE TO PRESSURE AND VOLUME LOADS, HEART-LUNG PREPARATION

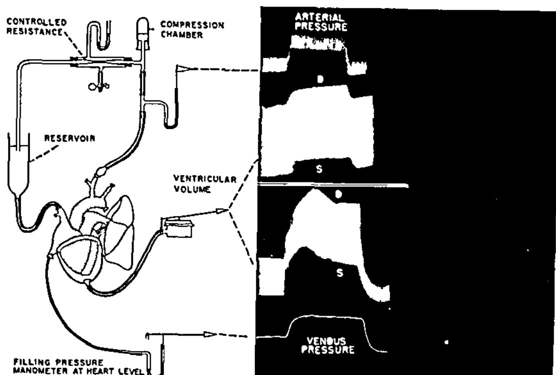


FIGURE 3 When exposed to an increase in work load (either increased stroke volume or increased arterial pressure) the ventricles in a heart lung preparation respond by distention to greater diastolic and systolic volumes Such experiments led Starling and his associates to postulate that the energy released by the contracting myocardium was determined by the initial length of the myocardial fibers as indicated by the end diastolic volume (After Patterson Piper and Starling[16])

Cardiac Response to Increased Systemic Arterial Pressure in the Heart-Lung Preparation

If the arterial pressure is suddenly increased, the systolic increase in intraventricular pressure is not sufficient to eject all the blood that entered during the previous diastole (Fig 3) The succeeding diastolic filling remains the same so an additional increment of blood remains within the ventricle The systolic and diastolic volumes expand until the energy released by the lengthened myocardial fibers is sufficient to meet the greater requirements for intraventricular pressure during each cycle

Starling's Law of the Heart

Starling and his associates[16] *confirmed the* general conclusions of Frank except for one crucial point, namely, that an increased diastolic volume was usually, but not always associated with a corresponding increase in filling pressure They stated ' We thus find no constant connection between the diastolic *tension and the succeeding contraction though as a rule these two quantities will be* altered together But we do find a direct proportion between the diastolic volume of the heart (i e the length of its muscle fibres) *and the energy set free in the following systole*

The law of the heart is therefore the same as that of skeletal muscle namely that the mechanical energy set free on passage from the resting to the contracted state depends on the area of 'chemically active surfaces i e, on the length of the muscle fibres [16]

According to these data the normal response to either a greater volume load or *pressure load is an increase in both diastolic and systolic* ventricular volumes A heart which becomes distended with a small or normal load is considered fatigued or depressed even though it may maintain a

anemia[20] arteriovenous shunts[19] and anxiety,[21] but the right atrial pressure in such patients was not elevated unless cardiac failure was present In patients with peripheral arteriovenous fistulae the cardiac output was lowered by temporarily occluding the fistula and returned to its former level on release of the pressure At these two greatly different levels of cardiac output the atrial pressure remained unchanged When atrial pressure was lowered by phlebotomy variations in cardiac output were produced but there was no consistent relationship with the magnitude of atrial pressure Release of tourniquets on the thighs produced a rise in atrial pressure without a consistent change in cardiac output [22,23] In all these studies intrapleural pressure was not measured so the conclusions are based on the assumption that differences in this variable were not significant. Barger et al[24] found that right atrial pressure in dogs usually diminished slightly with respect to atmospheric pressure during exertion sufficient to increase cardiac output fourfold or more However this was believed to be associated with an even greater reduction in mean intrathoracic pressure so the effective filling pressure may have actually increased

Cournand[25] has emphasized that small pressure changes in the right atrium may be associated with large variations in cardiac output (e g an increase in right atrial pressure of – mm Hg may be accompanied by a 40 per cent increase in cardiac output) Unfortunately specific data on changes in the effective filling pressure of the ventricular chambers under various conditions are so scarce that this matter must await further investigation

Changes in ventricular volume Although the traditional concepts of cardiovascular control appear to call for an increase in diastolic volume whenever the stroke volume is increased considerable evidence has been presented that the heart may be smaller during exercise (*vide infra*) Clearly this observation would not have been predicted from the experiments described above (*Fig* 3) One cause for such discrepancies is a change in heart rate (and diastolic interval) which may directly affect heart size [26] In addition, physiologic condition of the myocardium is subject to change under different circumstances Starling clearly recognized the importance of the functional state during both contraction and relaxation although it was not mentioned in his enunciation of the law of the heart He noted that so long as the pressure in the *inferior vena cava remained* low diastolic pressure in the ventricle depended essentially on the rate of relaxation of the ventricular muscle He stated [16] A slight change in the physiological condition of the heart muscle which might alter this rate of relaxation might therefore have a considerable influence on the actual diastolic pressure attained in the ventricle'

Changes in the Physiologic Condition of the Myocardium

Starling and his associates[16] reported experiments which demonstrated that stimulation of the vagus produced a prolongation of ventricular contraction and a slower rate of pressure rise They concluded that vagal stimulation slowed all the processes occurring in the ventricular muscle although it did not abolish the fundamental relation between length of muscle fiber and amount of energy released during contraction

It is generally recognized that epinephrine increases the vigor of myocardial contraction Wiggers[27] demonstrated that the intraventricular pressure rose more rapidly to greater heights and that systole was of shorter duration after administration of epinephrine A more direct study was accomplished in intact anesthetized dogs by means of cinefluorographic angiocardiography [28] The projected area of the ventricular chambers on successive motion picture frames was related to the effective filling pressure The diastolic area of the left ventricular chamber frequently increased without a corresponding alteration in effective filling pressure (*Fig* 4*A*) Epinephrine produced more complete systolic ...

dilatation in the muscles However, this is usually insufficient and cardiac output must increase to balance the diminished peripheral resistance and to sustain the arterial blood pressure The cardioregulatory centers promptly produce tachycardia, a step toward increasing the cardiac output At the same time, stroke volume must be expanded

Increased stroke volume depends upon an *increase in "venous return"* Compression of the veins by contracting skeletal muscles propels the blood in peripheral veins onward *toward the heart At the same time, greater* respiratory activity expresses blood from the splanchnic bed into the thoracic veins (Fig 7, Chapter 3) Central venous pressure is elevated so that the diastolic filling of the right ventricle is increased Right ventricular ejection is therefore increased and the larger blood flow through the lungs is rapidly reflected in an increased left ventricular stroke volume The circulation then becomes stabilized at a new, higher level of systemic blood flow This sequence of events illustrates how the accepted concepts of cardiovascular control are generally applied to a cardiovascular response However, even a superficial examination of these mechanisms reveals *gross* discrepancies

Appraisal of Fundamental Concepts Concerning the Cardiac Response to Exercise

Five mechanisms have been ascribed prominent roles in promoting increased cardiac output during exercise (*a*) a drop in arterial blood pressure (*b*) cardio-acceleration induced reflexly by pressoreceptors, (*c*) an increase in "venous return," (*d*) elevated central venous pressure and (*e*) increased diastolic ventricular volume leading to increased stroke volume

Arterial blood pressure is characteristically elevated during exercise If a drop in arterial pressure occurs at all, it is so transient at the beginning of exertion that it cannot be consistently demonstrated in man or experimental animals (see Figs 9, 10, 11, 12)

Tachycardia often occurs in anticipation of exertion, before muscular contractions begin During exercise the elevated arterial blood pressure should slow the heart What sustains the accelerated heart rate during exertion? Furthermore cardio-acceleration per se does not increase cardiac output With constant "venous return" the cardiac output cannot be increased by tachycardia

"*Venous return*" is a term which is widely used but rarely defined It appears to stem from experiments with heart-lung preparations in which an ample venous reservoir of *blood could be artificially maintained (Fig* 3) However, the intact circulation is a closed system A sustained increase in volume flow through the veins can only occur when the flow through the entire circuit has been correspondingly increased If increased venous return refers to an increase in the volume flow throughout the entire circulation it most certainly occurs during exertion On the other hand, if increased venous return implies a greater volume flow through the veins than in other portions of the circulatory system such an effect must be very transient indeed *Contracting skeletal muscle* and more vigorous respiratory activity can expel an increment of blood toward the heart only at the onset of exercise "*Increased venous return*" is an ambiguous phrase which should be abandoned or specifically defined Some authors have used this expression as though it implied an elevated central venous pressure or increased filling pressure of the ventricles

Increased ventricular filling pressure Although an increase in peripheral venous pressure during exercise has been repeatedly *demonstrated changes in* central venous pressure have been somewhat equivocal For example, Stead and Warren[19] described a number of experiments utilizing cardiac catheterization on humans demonstrating that a change in the pressure in the right atrium may not be the primary mechanism producing the normal variations in stroke volume For example, the cardiac output of the body at rest was elevated in patients with

to intensive experimental studies of a basic sort.

Sarnoff and his associates [9] have, at long last made definite steps toward quantitating factors which affect the physiologic condition of the myocardium Systemic blood flow (cardiac output minus coronary flow) was continuously recorded with a Potter electroturbinometer [30] Simultaneous measurements of pressures in the pulmonary artery aorta and right and left atria were employed to determine the work of each ventricle during changes in atrial pressure induced by infusion from reservoirs supported at various levels above the heart The stroke work was plotted against mean atrial pressure The plotted data called Starling curves are presented beside the length-tension curve of Frank to emphasize certain important differences (Fig 2) First a descending limb (i e a decrease in work with increased effective filling pressure) did not occur in the normal dog heart but did appear when the ventricular myocardium was compromised by such things as restriction of coronary flow Of greater importance was the shift *of the entire curve to* a lower level under these circumstances (Fig 2) In contrast administration of epinephrine shifted the curve upward and to the left indicating an increase in stroke work per unit of filling pressure which might be described as increased contractility' (Fig 2) From such studies Sarnoff and his colleagues have postulated that under various conditions a ventricle may describe many different ventricular function curves Further discrepancies between atrial pressure and ventricular energy release do not negate the Frank Starling relationship but indicate that the ventricle is functioning on another curve These investigations hold great promise for elucidating the extent to which various factors are *capable* of affecting cardiac function in controlled experiments Unfortunately they do not indicate what factors are actually involved in the cardiovascular adjustments in intact unanesthetized *experimental* animals and in man

APPLICABILITY OF DATA FROM ANESTHETIZED, THORACOTOMIZED ANIMALS

Within the limitations of their experimental methods the validity of data obtained by such outstanding investigators as Frank Starling Wiggers or *Sarnoff* is not questioned when applied to the conditions of their experiments However, deficiencies in the classic recording techniques must be recognized For example changes in ventricular volume are recorded with reasonable accuracy by a cardiometer even though the records may be distorted at the transition between systole and diastole by movements of the heart in and out of the cardiometer Unfortunately cardiometers measure the combined volume of the right and left ventricles and cannot be used to determine changes in volume of each ventricle individually Since the right and left ventricles are very different with respect to their anatomy geometric configuration and function (Fig 12 Chapter 1) changes in volume of one chamber could easily obscure reactions in the other Sarnoff and his associates have overcome this difficulty by recording blood flow from each ventricle Actually, the cyclic variations in absolute volume of individual cardiac chambers have never been directly measured in a *beating heart* Even if it were possible to measure accurately all the significant variables simultaneously in anesthetized thoracotomized animals, application of these data to normal animals and to man would require some rather broad assumptions

Effects of Anesthesia

Cardioregulatory influences *from the* higher centers of the central *nervous system* are undoubtedly depressed distorted or eliminated by *surgical* anesthesia Clearly, cerebral *effects* on cardiovascular control *cannot be studied* in anesthetized animals while in normal individuals they may play important roles Reflex mechanisms involving the lower *levels* of the nervous

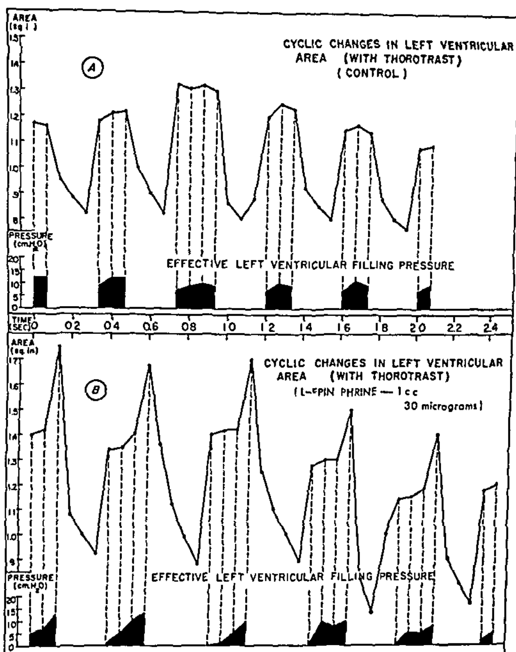


FIGURE 4 The relation between left ventricular size and effective filling pressure was investigated in intact anesthetized dogs utilizing cinefluorographic angiocardiography [28] The projected area of the left ventricular cavity was measured on successive frames from cinefluorographic films (see Fig 13 Chapter 1)

A The diastolic area of the left ventricle became greater when the effective filling pressure was slightly diminished in the third cycle Thus the diastolic volume was apparently not directly determined by effective filling pressure

B Epinephrine produced a reduction in effective filling pressure without a corresponding decrease in diastolic area of the ventricle and also produced progressively greater systolic ejection

tion Greater diastolic size was attained with a reduction in effective diastolic filling pressure (Fig 4*B*) which means that the resistance to distention was decreased An increase in "distensibility" by epinephrine had been previously described by Wiggers [27] In this connection Wiggers stated [14] 'The multiple factors which can separately influence the response of the myocardium at equivalent initial lengths must be submitted

tend to become larger in response to an increased load It seems possible that many of them could not have become smaller

VENTRICULAR RESPONSES IN INTACT UNANESTHETIZED ANIMALS AND IN MAN

One method for testing the applicability of a natural law is to determine whether it can be used successfully to predict a response under a specific set of conditions If Starling s law of the heart is the dominant factor in cardiac control in intact animals myocardial fibers should be stretched and the chambers should become larger whenever greater energy release occurs It might be predicted that the left ventricular chamber would be relatively small during rest while during exercise both the systolic and diastolic volume should be larger if the stroke work increases If predicted responses are not clearly demonstrable factors other than

SHRINKAGE OF THE EXPOSED HEART

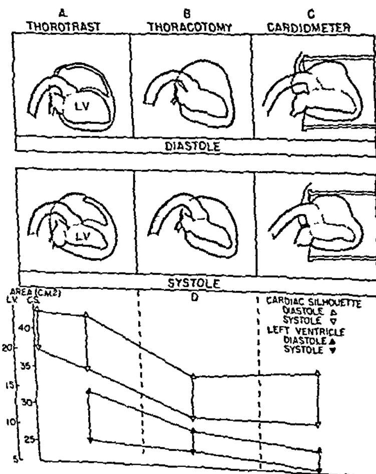


FIGURE 5 *A* Thorotrast was injected into a normal unanesthetized dog and its course through the heart was recorded cin fluorograph cally The area of the cardiac silhouette and of the left ventricle during both systole and diastole are indicated in the graph *D*

B After anesthesia and thoracotomy the heart definitely became smaller

C The cardiac silhouette changed in configuration when the heart was placed in a loose fitting cardiometer but its area was not diminished. The left ventricular area was further reduced by this procedure The left ventricle emptied almost completely at the end of systole a situation which never was encountered among intact dogs

system are also depressed or distorted by anesthesia Since the basic data which led to the traditional concepts of cardiac control were derived from controlled experiments it is not surprising that the mechanical aspects of the cardiac response have been emphasized with relatively little consideration of neural and hormonal influences

Experimentally Applied Loads on the Heart

The circulatory system of an anesthetized dog is stable In other words, nothing happens until some change is induced by the investigator Experimentally induced loads on the heart are presumed to be equivalent to naturally occurring functional loads For example, increasing cardiac output by rapid infusion of saline or blood from a reservoir may not be equivalent to the natural mechanisms for increasing stroke volume An increase in ventricular filling pressure is virtually assured by this procedure Increased filling pressure may be an important cardioregulatory mechanism, but it never acts alone in intact animals

Effects of Thoracotomy on the Heart

During the period when Starling conducted his classic experiments it was generally believed that the ventricles were almost completely evacuated by each systolic contraction under normal resting conditions This concept persists in the general attitude that a small heart is a normal heart—indeed, the smaller the better More recently relatively large volumes of residual blood have been demonstrated in normal ventricles at the end of systole The amount of residual blood in each ventricle, illustrated in Figures 9 and 13, Chapter 1 is typical of intact dogs [31, 32] Equally convincing evidence of residual blood has been obtained in man [33, 35] Kjellberg et al [36] demonstrated a close correlation between total blood volume and heart volume, and concluded that about 10 per cent of the blood volume is contained within the chambers of the heart

Ferguson, Shadle and Gregg[37] observed gross differences between the performance of the heart in open and closed chest dogs The average values for left ventricular diastolic pressure, stroke work index and stroke volume index in closed chest dogs were each more than four times that of open chest animals and the cardiac index was twice as great An important factor in reducing the stroke volume was the heart rate, which averaged three times greater in open chest animals (180 per minute) than in intact dogs (60 per minute)

Evidence has recently been presented that the heart shrinks in size in anesthetized thoracotomized animals [38] Cinefluorographic films were taken of the hearts of normal dogs lying unrestrained on the table Thorotrast (50 cc) was then injected intravenously and another film obtained Cinefluorographic records of the cardiac silhouette and heart chambers were then made after each of the following procedures (*a*) surgical anesthesia induced by intravenous Nembutal (*b*) thoracotomy and (*c*) the application of a cardiometer The area of the cardiac silhouette and of the left ventricular chambers consistently diminished (Fig 5) After the thorax was opened the left ventricular chamber often appeared to empty almost completely during each systole The heart remained very small for extended periods even after reinflation of the lungs and careful repair of the thoracotomy In one or two days, the heart generally regained the control dimensions (see also Fig 7*A*) Injection and withdrawal of air into the pleural space definitely affected the size of the left ventricle (Fig 15) The distention of the heart to the preoperative size appeared to be greatly accelerated by carefully removing as much air from the pleural space as possible It seemed that small quantities of air within the thorax significantly affected the degree and persistence of the abnormally small heart size after thoracotomy Thus the original cardiometer experiments were probably conducted on hearts which were very much smaller than normal Under these circumstances, it is not surprising that they would

mitted the extracardiac pressure to the opposite side of the diaphragm Thus, the transmural pressure across the left ventricular wall could be recorded along with changes in diameter or circumference (see Fig 6)

Although the variable inductance diameter gauges and pressure gauges are extremely accurate and reliable instruments, the effects of their installation could influence cardiac function For example pleural and pericardial adhesions form to varying extent in and around such foreign bodies in the chest The mercury filled rubber tubes are not as accurate as the inductance gauges although they appear to indicate qualitative changes with considerable reliability In spite of such potential sources of error the data derived from such measurements in intact dogs appear more applicable than data derived from experiments on anesthetized, thoracotomized animals

Changes in Left Ventricular Dimensions

The filling patterns were somewhat variable in different animals and in the same

RECORDING OF LEFT VENTRICULAR DIAMETER

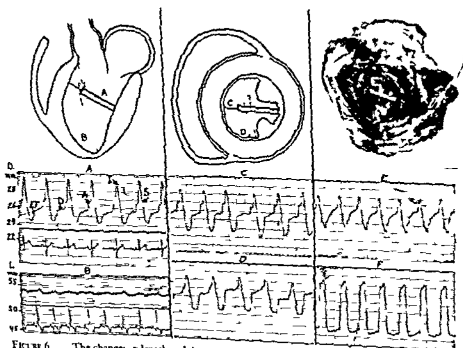


FIGURE 6 The changes n length and diameter of the left ventricular cavity were recorded continuously from intact un nesthetized dogs by means of variable inductance gauges
A The typ cal patterns of changing left ventricular diameter consisted of five phases (EF) early diastolic filling (D) diminished inflow or diastasis (A) atrial contraction (I) a sudden expansion of the diameter associated with isometric contraction of the left ventricle and (S) systolic ejection
B The length of the left ventricle between th root of the aorta and the apex, changed very little during the card ac cycle (increasing a little at the onset of ystole and diminishing slightly during late systole)
C and *D* Similar patterns were obtained from diameter gauges oriented roughly at 90 degrees in two different dogs This observation indicates that the left ventricle functions as a cylindrical chamber with concentri contraction of the walls
E and *F* Left entricular diameter measured simultaneously with left ventricular pressures indicated that the sharp sp ke on the diameter gauge record (I wa e) actually began during isometric contraction just as the ventricular pressure started to rise abruptly The pressure gauge was mounted at the apex of the heart with a small plastic tube extending into the lumen of the left ventricular cavity

those expressed in the law must be operating or even dominating the picture. Data on changes in the absolute dimensions of the heart in normal animals and man are relatively scarce, yet available information fails to confirm the generally accepted concepts in many respects.

In 1923, Meek and Eyster[39] described measurements of cardiac size and cardiac output by means of roentgenograms. They found that, during exertion, diastolic size of the heart increased in ten subjects and diminished in seven. The systolic size showed a decrease in 11 individuals and was larger in the other six. Since an increased output per beat was sometimes noted even though the diastolic size had decreased, the increased stroke could hardly have been caused by an increased length of cardiac fiber in the preceding diastole."

Sjostrand[40] reported that the heart volume of human subjects, measured roentgenographically, was greater when lying down than when standing or sitting. The effects of drugs like epinephrine, nor-epinephrine, atropine, nitroglycerin, and digitalis in toxic doses were studied in reclining subjects and the heart volume remained unaltered or was decreased but never became greater than before the administration of the drug. Even during arduous work on a bicycle ergometer, the heart volume was never greater than the reclining value and was usually smaller. Thus, under optimal conditions for heart filling (recumbency) the heart appeared to be filled maximally during diastole. The mechanism utilized by normal subjects to attain increased cardiac output has been related to both heart volume and total blood volume. For example individuals with large blood volume and large hearts (i.e., athletes) tend to increase cardiac output by greater stroke volume and less cardioacceleration in comparison with subjects with smaller blood volume and heart size. Unfortunately, such roentgenographic studies do not indicate the changes in volume of individual cardiac chambers.

Techniques for Recording Cardiac Performance in Intact Dogs

Although it has been impossible to measure directly absolute ventricular volume in intact animals, new techniques have been devised (41) for continuous recording of the circumference, diameter and length of the left ventricular chamber. Records have been obtained during a wide range of activities for periods as long as 26 days. The methods used for these studies are described briefly because they are recent developments which are not generally familiar. Data reported in the remainder of this chapter have been recorded by these means.

Left ventricular diameter has been measured by a variable inductance gauge installed within that chamber and connected on the outside to a recording device. The gauge comprises a coil anchored at one end to the free wall of the left ventricle, and a stylus, anchored to the mid-portion of the interventricular wall and free to move within the coil. The position of the stylus within the coil can be recorded to a fraction of a millimeter.

Left ventricular length was measured by a variable inductance gauge similar to that used to record diameter but installed between the root of the aorta and the apex of the chamber.

Left ventricular circumference was measured by a variable resistance gauge (a mercury-filled rubber tube) encircling the chamber (Fig. 7); a wire from one end of the gauge passed into the right ventricular cavity to follow the contour of the interventricular septum. The absolute circumference of the gauge was determined from roentgenograms exposed perpendicular to the long axis of the ventricle.

Effective left ventricular pressure was recorded by means of a small differential-transformer pressure gauge installed at the apex of the left ventricle. A short plastic tube inserted within the ventricular cavity, conducted pressure to one side of the gauge and a rubber balloon in the pleural space trans-

the ventricle re-expanded to the preoperative dimensions so that the complete cardiac cycle could be recorded The left ventricular diameter stabilized at levels slightly above or slightly below that illustrated in Figure 7*B* under different degrees of activity over a period of 22 days

When the heart re-expanded to its preoperative size (see Fig 7) the diameter was always more than 2 cm and the change during each cycle was only 0 6 to 0 8 cm These measurements provide further objective evidence that the left ventricle normally contains considerable blood at the end of systole and therefore functions at fairly large systolic and diastolic dimensions In contrast changes in left ventricular length measured by an inductance gauge installed between the root of the aorta and the apex of the chamber revealed shortening of less than 1 mm (Fig 6) Thus the septal wall of the chamber shortens only very slightly as was previously indicated by cinefluorographic studies (see Fig 11 Chapter 1)

Patterns obtained from diameter gauges installed at approximately 90 degrees in different animals were similar in form (Fig 6) This observation suggests that the left ventricular cavity is diminished concentrically during each systole All these observations led to the conclusion that the left ventricle functions like a cylindrical chamber and ejects blood primarily by concentric reduction of its circumference and diameter with little change in length The same concept had been previously suggested by studies of cinefluorographic angiocardiography (see Chapter 1) However the *free* walls of the right and left ventricular cavities shorten significantly during systole (Figs 11 and 12 Chapter 1) The volume of a cylindrical chamber varies directly with a change in length but is related to the square of the diameter Thus the changes in left ventricular circumference and diameter are more closely related to the stroke volume For this reason the left ventricular diameter and circumference have been selected for direct measurement while changes in length have been neglected in most of the studies considered below

The patterns recorded from circumference gauges on the day of operation were always very similar in form to the typical cardiometer records However during the next few days, the smooth diastolic curve gradually changed to resemble the typical records obtained with diameter gauges (Fig 7) The change in circumference (ranging from 2 5 to 5 mm) during each cardiac cycl was surprisingly small in almost all experiments

Stroke Work of Myocardial Fibers

Burch and Ray (see Fig 8 4) used typica records from Wiggers to plot ventricula pressure against ventricular volume, pro ducing a loop which describes the function o the ventricular chambers During diastol the volume increased while the pressur dropped slightly Isometric contractio produced a sudden rise in pressure with n change in volume During ejection th volume diminished while the pressure ro slightly Isometric relaxation permitted th pressure to fall abruptly with little change volume If the pressure and volume of a individual ventricle were used to constru such a loop the enclosed area would be direct expression of the ventricular stro work

A plot of pressure against diameter pr duced a loop which was similar in contour that obtained by Burch and Ray (Fig 8 If the diameter were directly proportional the volume the area of a pressure-diame loop would indicate the stroke work of entire left ventricle In recording the chan in pressure on the vertical axis of a catho ray oscilloscope and the variations in c cumference on the horizontal axis, e cycle produces a loop which is similar to other two in Figure 8 The area of suc loop does not indicate total ventricular w but it must be related to the work complished by the myocardial fibers wh contribute to the change in circumferen For the present

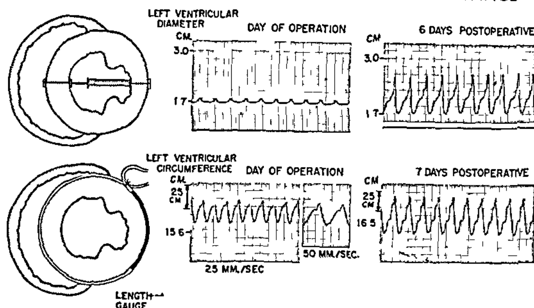


FIGURE 7 Left ventricular diameter was measured by means of a variable inductance gauge consisting of a small coil anchored to the free wall Within the coil was a magnetic steel stylus anchored to the interventricular septum On the day of operation the heart was characteristically so shrunken (see Fig 5) that the stylus was pressed within the coil during almost the entire cardiac cycle After a day or two the heart returned to its preoperative size and in this case the gauge recorded satisfactorily for 22 days

Changes in left ventricular circumference were recorded by variable resistance gauges consisting of a length of delicate rubber tubing filled with mercury One wire from the gauge followed the interventricular septum to encircle the left ventricular cavity On the day of operation the pattern closely resembled those obtained from cardiometers During the next few days the patterns changed and often were very similar to those recorded by diameter gauges

animal at different times Although changes in heart rate were an important factor in this variability in wave form, this was not the only factor The patterns of filling and emptying obtained from cardiometers are also quite variable and do not always conform to the familiar pattern described by Wiggers[17] as typical (see Fig 8) The variability of diameter and circumference patterns is no greater than that observed on cardiometer records obtained under different conditions

Left ventricular diameter and circumference patterns (Fig 6) are similar to the combined ventricular volume curves (Fig 8*A*) except for certain characteristic differences The increase in diameter during diastole generally occurred in several phases (*a*) The initial rapid filling phase was followed by a plateau (diastasis) or gradually rising slope of short or long duration depending upon the heart rate (*b*) A sharp increase in diameter followed atrial systole (*c*) A sharp spike was superimposed upon the top of the atrial deflection

The final sharp spike taking off from the top of the atrial deflection (I wave in Fig 6*A*) actually occurred during isometric contraction (Fig 6*E*, *F*) Tentatively this very abrupt increase in diameter was ascribed to a change in shape of the ventricular chamber due to a reduction in length with bulging of the lateral walls as the internal pressure built up In other words a cylindrical chamber might assume a more spherical configuration at the very beginning of systole

Records of left ventricular diameter and circumference are compared in Figure 7 On the day of operation the left ventricular chamber was so small that the stylus was pressed within the coil during all phases of the cardiac cycle except for the slight upward deflection at the moment of maximal expansion In this animal four days elapsed before

been selected as 'typical The results of these experiments are described more fully than would ordinarily be warranted because much of the material is not yet published elsewhere

RESPIRATORY ACTIVITY During normal respiratory activity, an increase in diastolic pressure was accompanied by an increase in diastolic and systolic diameter (Fig 9) The systolic pressure was also elevated The area of pressure-circumference loops was often increased when the diastolic pressure rose, but the changes were slight and not very consistent

CARDIAC RESPONSES IN AN INTACT DOG (LEFT VENTRICULAR DIAMETER)

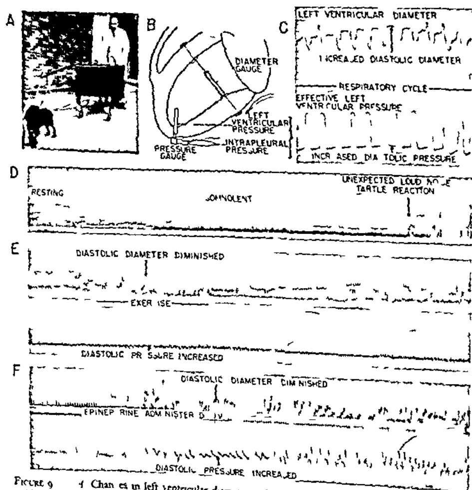


FIGURE 9 *A* Changes in left ventricular diameter and left ventricular pressure were inscribed by a portable recording device during many types of common activity

B The location of the diameter and pressure gauges are illustrated on a schematic diagram of the left ventricle

C During respiratory activity an increase in effective left ventricular diastolic pressure was characteristically associated with an increase in diastolic diameter

D During sleep the left ventricular diameter diminished to a remarkable extent returning abruptly to the normal waking range when the dog was rudely awakened by a loud noise

E During exercise the left ventricular diameter diminished and the diastolic and systolic pressures progressively increased.

F Epinephrine produced an increase in diastolic pressure and a reduction in diastolic diameter Systolic diameter was so greatly reduced that the gauge blocked during a considerable portion of the cardiac cycle.

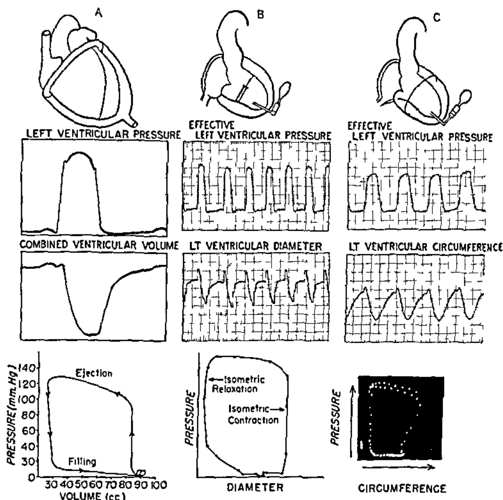


FIGURE 8 *A* When the left ventricular pressure is plotted against the combined ventricular volume obtained from cardiometer records a loop is produced which describes pressure volume relations of this complicated system If such a loop could be produced by plotting the pressure and volume of the left ventricle alone the area within the loop would represent the stroke work or energy release by the ventricle during a cardiac cycle (After Burch G E Ray C T and Cronvich J A Circulation 5 504–513 1952)

B A continuous plot of left ventricular diameter against left ventricular pressure produced a loop which bears some resemblance to the loop in *A*

C A continuous plot of left ventricular pressure against left ventricular circumference was recorded on the face of a cathode ray oscilloscope to produce a loop The area of these loops probably reflects the energy released by the myocardial fibers which contribute to the change in circumference being measured

indicate directional changes for which they appear very reliable If changes in circumference reflect changes in myocardial fiber length and pressure-circumference loops indicate the work accomplished by these fibers, the relation between the fibers length and their energy release (Starling's law) can be evaluated directly for the first time in intact animals

Changes in Left Ventricular Function during Everyday Activity

Records of left ventricular dimension and/or pressures have been obtained from some 76 animals over periods of days or weeks Although the number of experimental animals remains small because of great technical difficulties, voluminous data have been collected from each successful preparation, since many records could be obtained daily The response of the heart to any particular stress or situation differed among animals and in the same animal on different occasions Since it is impossible to describe all the variations of response the changes which were observed most frequently have

heart rate and ventricular diameter appeared during the first cycle after the stimulus The very rapid cardiac response to startle suggests that neural reflexes may directly affect heart size by changing the distensibility or contractility of the myocardium

CHANGES IN POSITION Spontaneous changes in left ventricular circumference and diameter generally occurred during any shift in position (Fig 10) For example the left ventricular dimensions tended to be somewhat smaller when the animal reclined with his head resting on the floor than when he was looking around Paradoxically the left ventricle was generally larger when the animal was alert while reclining than when he sat up The prompt changes in both pressure and circumference associated with standing sitting or walking spontaneously are clearly illustrated in Figure 10 If the animal remained quiet in any particular position the records became very stable

EATING On one occasion a dog was presented a plate of food and ate voraciously (Fig 10) His systolic and diastolic ventricular pressures progressively rose and the circumference also increased both in amplitude and during each diastole After eating he was encouraged to run 60 yards down the hall and the response was not only less than the usual reaction to exercise but was clearly no greater than occurred during eating Another dog exhibited a similar response while he emptied a plate of food Shortly thereafter the empty plate was placed before him and even though he evidenced little interest in it essentially the same effects on the heart were produced

EXERCISE A wide variety of responses to exercise has been observed in different animals and in the same animal under similar

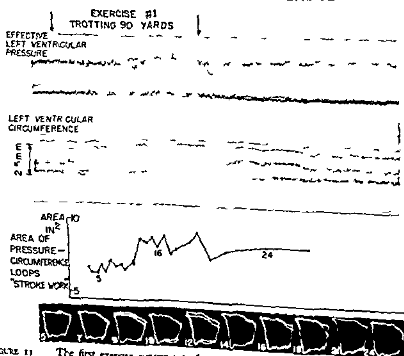


FIGURE 11 The first exercise experiment after the installation of the gauges consisted of trotting briskly (some 90 yards) down the hall of the building while connected to a portable recording device (see Fig 9A) The initial response was a reduction in both systolic and diastolic diameter followed by an increase in the diastolic dimension to a level slightly above the base line The systolic pressure did not increase promptly and the area of the pressure-circumference loops increased gradually This was a decidedly "atypical" response apparently because the animal did not know exactly what was expected of him (see Fig 12)

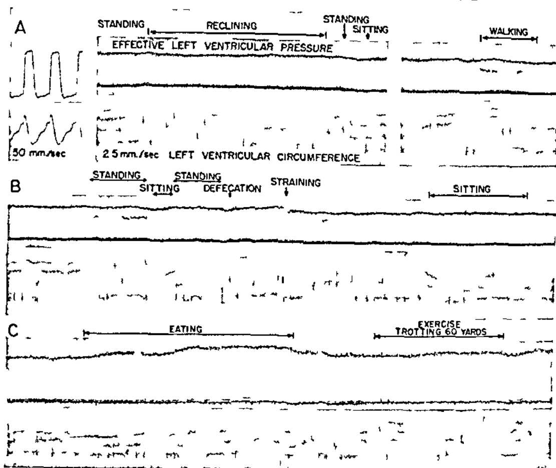


FIGURE 10 *A* Spontaneous alterations in left ventricular circumference and left ventricular pressure were recorded during changes in position and spontaneous walking Note that circumference was larger when the dog was lying down than when he was sitting

B, Left ventricular diameter and pressure altered during defecation and the restless activity which preceded defecation A marked transient reduction in systolic and diastolic circumference accompanied straining

C Eating produced very marked changes in both left ventricular circumference and pressure Indeed in this particular case the response to eating was greater than to exercise which immediately followed The response to this particular bout of exertion was much less than was ordinarily produced

SLEEP *Three dogs have fallen asleep* while connected to the recording equipment In each case, the systolic and diastolic dimensions (diameter or circumference) have diminished very significantly (Fig 9) The reduction in heart size during sleep was greater than during any other situation in the intact unanesthetized dog, but on no occasion reached the very small size encountered during and immediately after thoracotomy When the animal re-awakened, either *spontaneously or as a result of a loud* noise, the left ventricle promptly returned to the larger dimensions typical of the waking state

CARDIAC RESPONSE TO STARTLE An *unexpected loud noise produced a character*istic response consisting of a transient tachycardia and an increase in both the systolic and the diastolic left ventricular diameter [41] This is of particular interest on three counts (*a*) The ventricles are capable of distending beyond the control level, both during a startle reaction and following exercise (*b*) Tachycardia is generally believed to produce a diminution in ventricular volume, particularly under conditions which do *not involve increased metabolic requirements* yet the startle reaction characteristically induced a prompt increase in both systolic and diastolic diameters when the heart was accelerating (*c*) A change in

from these records, an increase in stroke volume can be attained by greater diastolic distention greater systolic ejection or both

ADMINISTRATION OF EPINEPHRINE. The effects of intravenous administration of levo-epinephrine (0 003 mg per kilogram) were quite variable The record in Figure 13 indicates the response in a dog still under the anesthetic in the post-operative period Since the changes in diastolic circumference were somewhat out of phase with changes in diastolic pressure the degree of diastolic filling could not have been determined solely by the effective filling pressure In other words, changes in distensibility of the myocardial fibers were probably involved (*vide infra*) Increased stroke volume was presumably attained first by greater systolic ejection and later by greater diastolic distention The area of the pressure-circumference loops ("stroke work") increased promptly owing to increased excursions of both pressure and circumference

In contrast with the experiment illustrated in Figure 13, the effects of epinephrine were quite different in another dog studied three weeks after operation (Fig 9) In this instance the diastolic ventricular pressure rose but the diastolic diameter diminished during the action of the drug The extent of systolic ejection was obscured by blocking of the gauge Kjellberg et al [42] studied the effects of epinephrine in humans and also found that the increase in stroke volume was due primarily to more complete emptying of the ventricles Since acetylcholine and epinephrine like substances may reach the heart simultaneously in the intact individual the combined effects of these agents deserve further study For example Kjellberg et al [43]

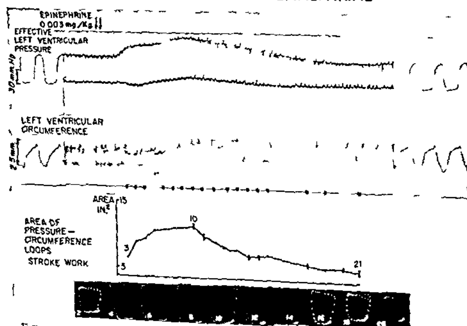


FIGURE 13 In an anesthetized dog following the installation of the gauges the initial response to epinephrine was an increase in ventricular systolic pressure which was abnormally low at the beginning Next the systolic circumference became smaller (more complete ejection) and the diastolic pressure diminished without a change in diastolic circumference The area of the pressure-circumference loops increased considerably during these adjustments Diastolic circumference then diminished slightly as the excursion became greater owing to markedly increased systolic ejection Systolic and diastolic pressure and systolic and diastolic circumference all rose more or less together The increased diastolic circumference persisted longer than the elevated diastolic pressure Considerable variability in the response to epinephrine has been encountered in different animals and under different conditions (see Fig 9F)

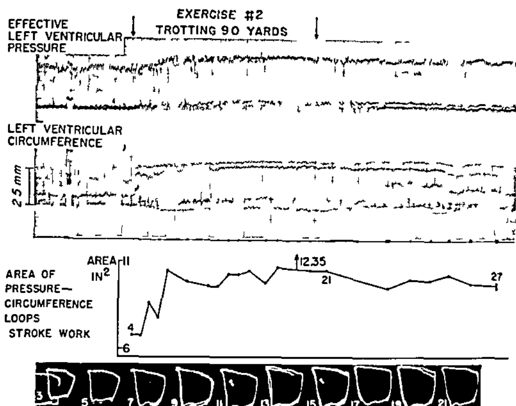


FIGURE 12 The second exercise experiment conducted a few moments later produced a response which was typical for this animal consisting of a prompt increase in ventricular systolic and diastolic pressures greater systolic ejection slightly greater diastolic filling and an abrupt increase in area of the pressure-circumference loops The remarkable difference between the first and second exercise experiments suggests that knowing what is expected has a significant effect on cardiovascular control and probably involves powerful influences by the central nervous system

conditions For example, the first bout of exercise in one dog elicited the changes illustrated in Figure 11

Within five minutes, the second exercise experiment was carried out under the same conditions (Fig 12) In this case both the systolic and diastolic ventricular pressures increased much more promptly The diastolic circumference increased progressively even though the diastolic pressure remained at about the same level The systolic circumference was reduced more promptly and to about the same extent as before The area of the pressure-circumference loops increased very promptly and was well sustained throughout the exercise and afterward If the pressure-circumference loops indicate changes in the work done by the myocardial fibers under the gauge, the stroke work by these fibers increased much more promptly on the second experience with exercise than on the first All subsequent exercise records conformed closely to exercise number 2 (Fig 12) and none revealed the delayed response indicated in Figure 11

Occasionally stroke volume was increased by two different mechanisms in the same dog on successive trials In one instance, the diastolic circumference remained about the same and the systolic reduction in circumference was greater In the second, the systolic circumference remained about the same and the diastolic circumference increased markedly In either case, diastolic pressure increased to approximately the same extent On many occasions, the heart responded to exercise by a reduction in both diastolic and systolic diameters in spite of an elevated diastolic pressure (Fig 9) Judging

Energy Release by the Myocardium

Since the pressure-circumference loops (Fig 8) reflect variations in the work accomplished by the myocardial fibers factors which affect energy release by the myocardium can be examined First let us consider the area of pressure-circumference loops in relation to the length of the myocardial fibers (circumference of the ventricle) During exercise the diastolic pressure, diastolic circumference and area of pressure-circumference loops all increased more or less simultaneously in Figure 12 However it is worth noting that the increase in stroke work appeared to be due primarily to a greater systolic ejection Further a major portion of the increased energy release was due to increased systolic pressure in the left ventricle Clearly the cardiac response to exertion cannot be explained by a simple relationship between diastolic volume and ventricular energy release as suggested by the usual application of Starling s law of the heart (Fig 14) Indeed, in many experiments diastolic dimensions of the ventricle diminished during both exercise and the administration of epinephrine (see Fig 9) The length of myocardial fibers and their energy release often changed in opposite directions

Perhaps the most obvious dissociation between diastolic size and energy release occurred during the intrapleural injection and withdrawal of 500 cc of air in a dog under anesthesia about 2 hours after the operation (Fig 15) Not only did the diastolic circumference diminish during an increase in effective diastolic pressure, but during withdrawal of the air the left ventricular circumference expanded to a level above that during the control period even though the energy release was definitely reduced

Thus multiple and interdependent mechanisms are probably involved and no simple generalization will explain cardiac control This indicates that changes in the functional

EFFECTS OF PNEUMOTHORAX ON CARDIAC ACTIVITY

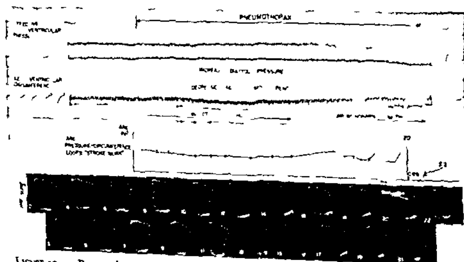
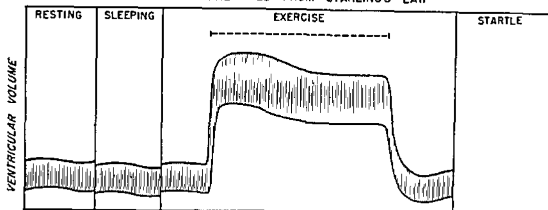


FIGURE 15 *Pneumothorax* was produced by intrapleural injection of 500 cc. of air in 50 cc increments The intrapleural pressure increased quite abruptly with the first increment of air and no change in diastolic circumference was noted until about 200 cc had been injected. Then the diastolic circumference diminished markedly as diastolic pressure increased slightly As the air was withdrawn from the thorax, diastolic circumference increased even after the diastolic pressure diminished and attained a level considerably higher than during the control interval. Pressure-circumference loops revealed little or no correlation between diastolic circumference or diastolic pressure with energy release A premature contraction produced a very small loop and the succeeding cycle produced a very large loop primarily because of markedly increased systolic ejection

RESERVE CAPACITY OF THE VENTRICLE



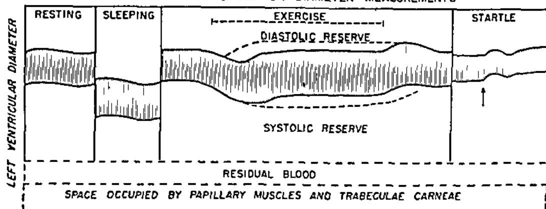


FIGURE 14 *A* Judging by experimental observations on heart lung preparations (Fig 3) the ventricles should respond to either a pressure load (increased arterial pressure) or a volume load (increased venous return) by *expansion to greater systolic and diastolic volumes* Since both increased stroke volume and increased arterial pressure occur during exertion the increased energy release should be attained by greater diastolic distention This type of response has never been observed during exertion in any experiment on intact, unanesthetized dogs

B In intact animals (and man) the ventricles function at large systolic and diastolic size at rest During sleep the ventricular size diminishes (see Fig 9) During exercise increased stroke volume appears to be attained by greater systolic ejection greater diastolic distention or both On this basis it is convenient to indicate a diastolic reserve capacity which is limited by maximal diastolic distention and a systolic reserve capacity which is determined by the maximal systolic ejection Both of these reserve capacities are utilized under various conditions *The term residual blood might well be used to describe the volume of blood remaining in the ventricular cavity after a maximal systolic ejection* Corresponding terms are now used to describe respiratory function and have the same logical basis

found that vagal blockade produced changes similar to those of injected epinephrine but had a much greater effect on the heart rate and blood pressure than on the contraction of the heart Peterson[44] reported that bradycardia produced by pressure on a sensitive carotid sinus was accompanied by less forceful contraction in spite of an increased diastolic filling interval He presented data which indicated a direct vagal influence on the contractility of the ventricle According to Hamilton[45] sympathetic stimuli accelerate the heart, augment its strength of beat and cause it to empty more completely An opposite effect results from parasympathetic stimulation He stated his belief that reflex mechanisms so completely dominate cardiac function that the heart does not appear to respond in accordance with Starling s law of the heart

Myocardial Distensibility

If a hollow viscus always has the same volume-pressure relationships the contained volume is determined solely by the effective pressure (see Fig 6*A* Chapter 2) On the contrary a large number of experiments have demonstrated that the diastolic dimensions may diminish during increased effective ventricular pressure or vice versa (e g Figs 9 13 14) These observations indicate that the resistance to stretch (distensibility) of the ventricular walls can be altered Changes in ventricular distensibility from beat to beat are also indicated by the pressure-circumference loops The bottom margin of each loop represents a continuous plot of the diastolic pressure and diastolic circumference If the distensibility of the myocardium remained absolutely constant the filling phases should produce lines which are precisely superimposed on one another This actually occurred in a few dogs while they rested quietly but was not the typical picture Superficial examination of the records indicated changes in diastolic pressure often without very obvious changes in filling pattern (Fig 16) When the sensitivity of the pressure recording channel was increased (Fig 16) the diastolic filling line varied from beat to beat indicating changes in distensibility of the myocardium Examination of the pressure-circumference loops in other examples confirmed this observation in an overwhelming proportion of the experiments (e g Figs 11 12 13 15 16) Perhaps the most striking example was the great change in left ventricular circumference associated with intentional pneumothorax (Fig 15) Such changes in distensibility permit the heart to assume large diastolic dimensions without increasing the filling pressure or the venous pressure upstream The functional significance of variable distensibility is considered in Chapter 7

SUMMARY

So long as the arterial blood pressure remains constant, the cardiac output must precisely balance the outflow of blood through all the capillaries of the systemic circulation The pressoreceptor mechanisms monitor the arterial blood pressure and influence both cardiac output and total peripheral resistance to maintain this equilibrium between inflow and outflow of the arterial system The sites of controlled resistance directly affect the blood flow through the vascular networks in response to both local metabolic activity and reflexes The increased cardiac output which must accompany reduced peripheral resistance during exercise is generally explained in terms of four factors (*a*) peripheral vasodilatation, (*b*) a drop in arterial blood pressure which reflexly produces compensatory vasoconstriction in inactive areas, (*c*) tachycardia produced by the same mechanism, (*d*) increased "venous return", and (*e*) greater diastolic distention of the ventricles However, these mechanisms do not fully explain the circulatory response to exercise The experimental data which led to the basic concepts of cardiac function and control were obtained under abnormal conditions The recording techniques such as cardiometry have inherent deficiencies The control exerted by higher levels of the central nervous system cannot be studied in anesthetized experimental animals The heart shrinks significantly following thoracotomy For these reasons the traditional concepts of cardiac function and control may not be applicable to unanesthetized animals and to man

Objective recordings of left ventricular dimensions and effective ventricular pressures have revealed that no simple generalization or law can explain the responses observed in intact dogs Many of these observations are consistent with comparable measurements on man It seems clear that the traditional explanations of cardiac function and control are highly oversimplified primarily because they were based on controlled experiments It now seems necessary to recognize that regulation of the heart involves multiple interacting mechanisms

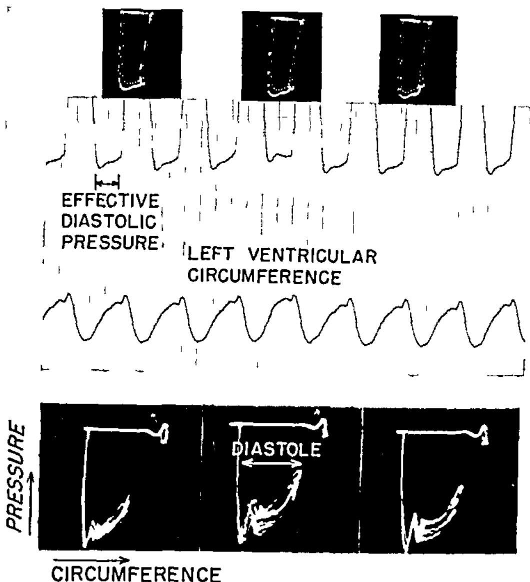


FIGURE 16 If the distensibility of the ventricles remains constant the circumference should always attain the same size for a particular level of effective diastolic pressure Thus the pressure-circumference curve should always follow exactly the same line during successive cycles Greater amplification of the pressure recordings reveals that both the course and the shape of the lower segment (diastole) of the pressure-circumference loops varies considerably from beat to beat The spread of these traces appears to be an expression of changes in myocardial distensibility

state of the myocardium (e g, contractility and distensibility) may play a dominant role in cardiac regulation under many different circumstances

Myocardial Contractility

Whenever the ventricles perform more work or eject more blood predominantly by greater systolic ejection, it seems reasonable to assume that the myocardial contractility is increased Examples have been presented illustrating this phenomenon during exercise (Figs 9 12) and after administration of epinephrine (Figs 9 13) When the degree of ventricular ejection is diminished without changes in other conditions, contractility is presumably reduced A detailed consideration of the factors which influence myocardial and ventricular contractility is presented in Chapter 7

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which vary heart rate, diastolic filling pressure, arterial blood pressure, myocardial contractility and myocardial distensibility Since changes in the "physiologic condition" of the myocardium have long been recognized but never assigned a prominent role in cardiac control, some of the factors affecting distensibility and contractility are considered in detail in Chapter 7

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forms of muscle and mechanisms by which neural and humoral factors could directly affect contraction and distention of the cardiac chambers. Some mechanical and architectural features of the ventricles will receive attention because they also may affect the function of the heart as a pump.

THE CONTRACTILE MECHANISM

The cardiac chambers are enclosed by walls consisting of bundles and sheets of myocardial fibers (Fig. 1). The individual myocardial fibers form a syncytium (Fig. 1*B*) which provides protoplasmic continuity between adjoining fibers and throughout an entire mass of cardiac muscle. Packed within the individual myocardial fibers are tremendous numbers of myofibrils. Examined under higher magnification (Fig. 1C) the myofibrils display the same cross-striations which appear in the parent fiber. The delicate myofibril is, in turn, a bundle of myofilaments which can be observed easily only with the electron microscope (Fig. 1*D*). The myofilaments have periodic beading but no other characteristic which would account for the cross-striations in the myofibrils. The myofilaments consist principally of the fundamental contractile units (Fig. 1*E*).

The Nature of Contraction and Relaxation

A multitude of theories have been evolved to explain the contraction and relaxation of muscle. It is not appropriate to plunge deeply into this rather chaotic subject, but a superficial consideration indicates the great similarity among the contractile mechanisms in smooth muscle, myocardium and skeletal muscle.

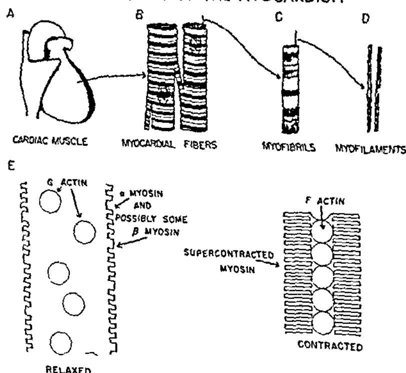


FIGURE 1 The heart walls are composed of sheets and bundles of myocardial fibers with protoplasmic continuity providing a syncytial arrangement. Myofibrils are packed within myocardial fibers. Myofibrils consist of myofilaments made up of fundamental contractile units. Transition from relaxed to contracted state is presented schematically. (From Astbury. Proc Roy Soc Lond. B137 58-63 1950.)

Chapter 7

Factors Affecting Ventricular Distensibility and Contractility

In Chapter 6, the traditional concepts of cardiac function and control were critically appraised. These concepts were originally based on controlled experiments on anesthetized experimental animals, and a reasonable doubt exists concerning their applicability to intact animals and man. Since an understanding of the principles governing cardiovascular responses in the normal individual is a prerequisite for interpreting changes induced by disease, additional factors which might affect cardiac function will be considered. The five basic mechanisms by which cardiac *output can be adjusted* are indicated in Table 1. The cardiac *output is determined by the product of heart* rate and stroke volume. Stroke volume is *determined by the diastolic volume of the* ventricle minus the volume of blood in the ventricle at the end of systole. Diastolic filling is determined by the effective filling pressure and the resistance to distention offered by the ventricular wall. Systolic ejection is determined by the arterial blood pressure and the degree of myocardial shortening which can occur against that particular outflow pressure. Of the five factors listed in Table 1, the traditional concepts emphasize only three: heart rate, ventricular filling pressure and arterial blood pressure. The distensibility and contractility of the ventricular walls represent changes in the "physiologic condition" of the myocardium discussed in Chapter 6.

The well established effects of epinephrine and acetylcholine on the myocardium suggest that direct neural and humoral control of the stroke volume could be attained by al*terations in contractility and distensibility*. This view is strengthened by the prompt and *unexpected changes in left ventricular diam*eter recorded in intact, unanesthetized *dogs described in Chapter 6*. The concept that direct neural and humoral factors can influence stroke volume has not been widely accepted. Perhaps this is partly due to difficulty in visualizing how neural or humoral influences could directly affect either diastolic filling or systolic ejection because changes in the characteristics of the contractile mechanisms would be involved. The following discussion will be devoted to a consideration of the basic contractile mechanism, the relation of myocardium to other

TABLE 1. MECHANISMS FOR INCREASING CARDIAC OUTPUT

Cardiac output ↑			
1. Heart rate ↑	Stroke volume ↑		
	Diastolic filling ↑		Systolic ejection ↑
	2. Effective filling pressure ↑	3. Myocardial distensibility ↑	4. Myocardial contractility ↑	5. Arterial blood pressure ↑

resembling incomplete tetanus in skeletal muscle. The response to injection of epinephrine is similar to that produced by a single nerve volley. Thus multiunit smooth muscle resembles skeletal muscle in many aspects of its excitation and control.

In contrast visceral smooth muscle, in the ureter, uterus and gastro-intestinal tract, is not directly innervated by motor nerves (Fig.). Waves of excitation originate in the muscle fibers and are conducted throughout the contiguous cells. Although protoplasmic continuity between adjacent cells cannot be clearly demonstrated, a mass of visceral smooth muscle functions like a syncytium so that excitation originating at one site may spread to all other portions. In the ureter, pacemaker activity is well developed at a point near the hilus of the kidney. Waves of excitation originate at this point at fairly regular intervals and proceed in an orderly fashion down the length of the tube. Thus the electrical activity of visceral smooth muscle is similar to that of the myocardium but very different from that of skeletal muscle (Fig. 2). Visceral smooth muscle is controlled by the autonomic nervous system principally *through the release* of hormonal substances rather than through direct motor innervation. *Thus*, visceral smooth muscle is closely related to myocardium so far as its excitation and control are concerned. If the completeness *of* contraction or relaxation can vary in smooth muscle there is no a priori reason for discarding this possibility in the myocardium.

The similarity of the basic contractile mechanisms is emphasized by the fact that apparent differences among the various types of muscle can be largely eliminated under specific conditions. For example, tetanus can be produced in papillary muscle from a mammalian heart maintained at 27° C. and electrically stimulated at a rapid rate.[6] A skeletal muscle deprived of its motor nerve

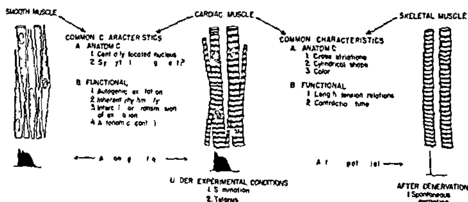


FIGURE 2. Properties common to visceral smooth muscle and myocardium are listed between schematic drawings of these fibers. Functional characteristics shared by myocardium and skeletal muscle are *similarly indicated between drawings*. These different types of fibers are *distinguished by their controlling mechanisms*, the fundamental contractile process being very similar in each type. As far as control is concerned, myocardium is more closely related to visceral smooth muscle than to skeletal muscle. Schematic representations of action potentials from three *types of muscle are indicated at* the bottom of respective drawings. Smooth muscle has a rapid depolarization which is sustained for an extended period and may have multiple superimposed spikes (After Bozler[4,5]). Myocardium tends to remain depolarized for a period approximately equal to the duration of contraction. In contrast, *skeletal muscle rapidly recovers* its polarization after excitation and responds to repetitive stimulation to produce sustained contractions. Under experimental conditions summation and tetanus can be produced in myocardial *fibers even though such* a response is usually considered characteristic of skeletal muscle. Denervated skeletal muscle exhibits spontaneous autogenic excitation (fibrillation) which is the typical form of excitation in myocardium and visceral smooth muscle.

According to Szent-Gyorgyi,[1] the fact that resting muscle is soft and pliable indicates that the contractile matter is composed of relatively short colloidal particles, contracted muscle is hard and tense as though it were constructed of long, stiff threads He believes that the contractile elements are fabricated from two very different substances (*a*) myosin, a protein consisting of relatively short molecular "rods," and (*b*) actin, a long continuous thread which has been compared with a chain of little round balls to account for its flexibility Neither of these components will contract independently However, actomyosin, a combination of the two substances, can be induced to contract by dipping it into boiled muscle juice The essential substances extracted from a boiled muscle are potassium ions, magnesium ions, and adenosine triphosphate (ATP)

According to Szent-Gyorgyi's recent description[2] of the contraction cycle, actin myosin, and ATP are all present, but dissociated, in resting muscle As a wave of excitation passes along the muscle membrane,' the balance of electrical charges is disturbed sufficiently to allow the actin and myosin-ATP to join and form actin-myosin-ATP In other words, excitation results in the formation of actomyosin which is unstable in its extended initial state, and which immediately begins to dissipate energy in the form of either increased tension or shortening The actomyosin is thus converted to its energy-poor state, and, in the process may accomplish work

If the muscle shortens during contraction, the heat production is far greater than it is during isometric contraction,[3] indicating that some of the energy released by the muscle is expended to overcome internal friction within the muscle (*vide infra*, "viscosity") If shortening could be completely prevented (isometric contraction) probably no energy would be expended at all because no work would be accomplished The complex could then dissociate again without splitting ATP, provided the resting ionic balance was restored The mechanism of relaxation remains controversial It has been proposed that dephosphorylation of ATP to ADP could produce relaxation and restoration of the energy-rich state before the next contraction Theories of this sort are in a constant state of flux and none can be considered a final answer in any sense of the word

The actin and myosin of skeletal muscle, myocardium, and smooth muscle are interchangeable, actin from one may combine with myosin from another to produce contractile actomyosin While there are some differences among the actomyosin complexes in the various types of muscle (digitalis glucosides have greater effect on the contraction when the actin is derived from heart muscle), the contractile mechanisms appear to be very closely related wherever found

The Relation of Myocardium to Other Types of Muscle

Since the contractile mechanisms are similar in different types of muscle, the principal functional differences are due to the mechanisms for excitation and control Because myocardium superficially resembles skeletal muscle in its cross-striations and color, and in the speed, vigor and duration of its contraction, the common tendency is to assume that cardiac muscle is only slightly different from skeletal muscle On the contrary in its functional characteristics and control, the myocardium more closely resembles visceral smooth muscle (Fig 2) Smooth muscle has been classified by Bozler[4,5] into two main divisions, (*a*) multiunit smooth muscle and (*b*) visceral smooth muscle Multiunit smooth muscle in the peripheral vascular system and the bladder, is directly innervated by motor nerves originating in the autonomic nervous system just as skeletal muscle is directly innervated by motoneurons The individual muscle fibers contract in response to impulses arriving along these nerves However, a single impulse may produce a sustained elevation in tension

pounds from the circulating blood Raab and Lepeschkin stated[8] 'An increase of the concentration of epinephrine-like substances in the heart has been observed colorimetrically not only after injection of epinephrine but also after physical exercise exposure to cold and administration of agents which are known to elicit the discharge of epinephrine and nor-epinephrine

The Effects of Epinephrine on Myocardial 'Distensibility

The rate at which blood enters the relaxed ventricular chambers depends upon the effective filling pressure the resistance to distention offered by the ventricular walls and the rate of inflow from the atria which is in turn related to the gradient in pressure from atria to ventricles When the diastolic filling slows or stops after the rapid filling phase the diastolic volume is determined principally by the effective filling pressure and the resistance to distention by the ventricular walls These two factors can be combined for convenience and expressed as "distensibility of the ventricles—*the diastolic volume per unit of effective filling pressure* If the diastolic volume increases when the filling pressure falls the distensibility is increased An increase in distensibility should facilitate diastolic filling in all phases of diastole The fact that epinephrine may increase distensibility has been well established[11 14] After studying the cardiodynamic effects of epinephrine Wiggers[11] arrived at the following conclusion Restated the diastolic volumes of the ventricles can be increased beyond their normal capacity (1) by an increased initial pressure overcoming the inherent tendency of the ventricles to resist stretching or (2) by a reduction of this inherent power of the ventricles to resist stretching i e by a

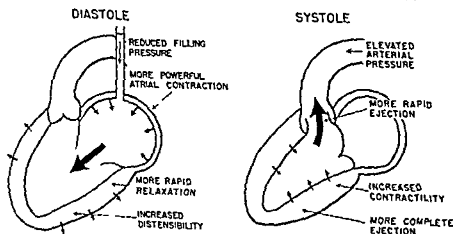


FIGURE 3 Epinephrine apparently affects cardiac function in several ways under different circumstances More rapid myocardial relaxation favors rapid inflow of blood during the early diastolic interval. Increased distensibility produces greater filling per unit of filling pressure which may result in either greater diastolic distention or diminished filling pressure during the mid-diastolic period (diastasis or slow filling interval) More powerful atrial contraction produces a greater filling pressure in late diastole and increases the volume entering the ventricle just before subsequent contraction.

During ventricular systole myocardium *contracts* more vigorously ventricular pressure rises more abruptly and ejection of blood is more complete *even though* arterial pressure is higher (increased contractility)

supply exhibits fibrillation due to myogenic impulses which spread along the individual fibers to produce asynchronous contractions This phenomenon can be directly observed on the surface of the tongue after degeneration of its motor nerves

THE BASIS FOR NEURAL AND HUMORAL CONTROL OF *MYOCARDIAL CONTRACTION* AND RELAXATION

The autonomic nervous system exerts its control over both visceral smooth muscle and myocardium by releasing acetylcholine and epinephrine Before the thesis that substances released by autonomic nerves can directly affect stroke volume is proved acceptable, the following requirements must be met (*a*) The existence of mechanisms for delivering epinephrine or acetylcholine to the myocardium must be established, (*b*) the occurrence of epinephrine or acetylcholine in the ventricular myocardium must be demonstrated, and (*c*) an effect of epinephrine or acetylcholine on the "distensibility" and "contractility" of ventricular myocardium must be demonstrated

Autonomic Innervation of the Heart

Nerves from the sympathetic system are widely and profusely distributed to all regions of the atrial and ventricular walls (Fig 1, Chapter 6) These nerve endings secrete epinephrine or epinephrine-like substances Thus, the ventricular myocardium is unquestionably exposed to epinephrine released by nerve endings within the ventricular walls as well as in the circulating blood Epinephrine released by the adrenal glands reaches all parts of the ventricular myocardium through the coronary vessels Greater quantities of epinephrine are released by the adrenal glands under those conditions of stress which are characteristically accompanied by increased stroke volume

Since acetylcholine reaching the blood from vagal nerve endings is apparently destroyed very rapidly, the quantity of circulating acetylcholine may not be sufficient to affect the ventricular myoca directly There is functional evidenc cardiac branches of the vagal nerve a distributed to the ventricular walls, be stricted to the atria, the S-A node, th node, the bundle of His and the b branches For example, stimulation vagus nerves has a powerful effect on e *pacemakers in the atria, but does n* fluence similar pacemakers in the ven (e g , complete heart block, parox *ventricular tachycardia) However, the* supply to the coronary arteries appears clude a large complement of vagal fiber deed, Essex and his colleagues[7] demons that control of the coronary vessels i diated principally by the vagus nerv these parasympathetic nerve endings the coronary vessels release acetylch this substance may well diffuse directly myocardial fibers In this case, the conce tion of acetylcholine will be greatest the coronaries are constricted and least they are being widely dilated by rec vagal "tone" in the area Thus, the least centration of acetylcholine and the gr quantity of epinephrine-like subst should occur when the heart is working der conditions promoting generalized pathetic discharge and vagal inhibition

Evidence of Epinephrine like S*stances within the Ventricular W*

There is ample evidence that substa present in the ventricular walls have p erties very similar to those of epinep and particularly of nor-epinephrine Ca "sympathin or its immediate precurs probably formed within the ganglia and p ganglionic fibers of the cardiac sympath nerves[8] Stimulation of these nerves creases the myocardial sympathin con tration[9] and cardiac denervation produc partial depletion of these substances[10] fact that denervation fails to produce c plete depletion indicates that neurosecre structures also exist inside the heart its Finally, the heart muscle absorbs and cumulates epinephrine and related c

changes in myocardial distensibility and contractility provide mechanisms by which the cardiac output can be increased without the changes in venous and arterial pressure which figure so prominently in the traditional explanations of cardiovascular response and which are so difficult to demonstrate in intact animals and man

It is convenient to label the quantity of blood remaining in the ventricle at the end of systole as the "systolic reserve volume" (Fig 4) Similarly the additional quantity of blood which could be accepted by the ventricle during maximal diastolic filling can be labeled the "diastolic reserve volume" The term "residual ventricular volume" could then be defined as the small quantity of blood remaining in the ventricle after maximal systolic ejection These terms correspond to those employed in describing lung volumes and have the same logical basis and similar functional significance In intact dogs left ventricular stroke volume is increased during exercise by utilizing the diastolic reserve the systolic reserve or both.

The presence of a diastolic reserve volume under resting conditions indicates that diastolic filling is arrested before maximal ventricular distention The factors which limit the degree of diastolic filling and myocardial stretch under various conditions influence the utilization of the diastolic reserve volume Similarly, the fact that on some occasions, greater systolic ejection can be accomplished by greater myocardial shortening emphasizes the importance of factors which arrest systolic ejection before the ventricles are emptied In fact, the control of stroke volume should be approached by considering the factors which promote or impede diastolic distention and systolic ejection Some of the factors included in the following discussion are not generally considered in this regard and deserve attention even though the available evidence is inadequate to indicate their relative importance

The Response of Myocardial Strips

The heart is composed of intricately interwoven bundles of myocardial fibers Cardiac contraction represents the sum total of their individual contributions For this reason the functional characteristics of strips or bundles of myocardial fibers is a primary consideration in this analysis

The tension developed by myocardium

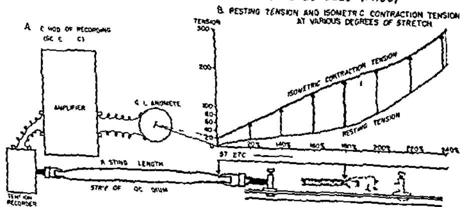


FIGURE 5 A Schematic diagram of experimental conditions employed by Lundin 15
B Tension developed by a strip of frog myocardium was recorded as it was stretched from its "resting length" to 240 per cent of resting length with isometric contraction tension recorded at various degrees of stretch. The maximum contractile tension occurred at about 180 per cent of "resting length"

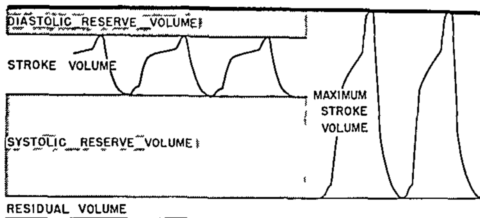


FIGURE 4 Judging from measurements of left ventricular diameter and circumference stroke volume can be increased by greater diastolic distention by more complete systolic ejection or by a combination of the two On this basis it is convenient to visualize a diastolic reserve volume and a systolic reserve volume the magnitudes of which depend upon the systolic and diastolic dimensions at any particular time The residual volume is the quantity of blood which remains in a ventricular chamber at the end of the most complete ejection of which it is capable Systolic reserve tends to be utilized predominantly when the heart is large before the onset of exercise and the diastolic reserve comes into play if the heart is smaller

reduction in their tonus Under normal conditions the former mechanism operates, under epinephrine the latter mechanism not only enters but predominates" Increased distensibility of the left ventricle is illustrated in Figure 4, Chapter 6 The injection of epinephrine resulted in diminished effective filling pressure and increased diastolic filling The greater ventricular filling during atrial systole was probably due in part to the greater "contractility of the atrial myocardium due to the presence of epinephrine

The Effects of Epinephrine on Myocardial "Contractility"

The term "contractility" is rather difficult to define in specific terms Wiggers[11] has shown that epinephrine exerts a stimulating action on the ventricles producing a faster pressure rise, a higher maximum systolic pressure and a shorter systole It also generally causes a more complete systolic ejection (Fig 3) For purposes of discussion, "improved contractility" will be used to denote a faster, more vigorous and more complete myocardial contraction These effects of epinephrine are widely recognized but are not usually considered in relation to the control of stroke volume However if sympathetic discharge is produced by either emotional states or intrinsic reflex mechanisms, the release of epinephrine unquestionably affects the stroke volume through change in the responsiveness of the myocardium (see Chapter 6)

THE FUNCTIONAL SIGNIFICANCE OF CHANGES IN "DISTENSIBILITY" AND "CONTRACTILITY"

Under normal resting conditions the ventricular chambers are neither emptied completely during systole nor filled to their maximum capacity during diastole For this reason, increased stroke volume can be attained either by more complete *systolic ejection* or by greater diastolic distention If the distensibility of the ventricular chambers is increased under neural and hormonal control the stroke volume can increase without *necessitating a corresponding* elevation of effective filling pressure Similarly, more complete systolic ejection through greater 'contractility of the myocardium could augment stroke volume without corresponding changes in effective filling pressure or arterial blood pressure In other words,

cardium produces a fall in contraction tension as soon as shortening begins If this viscosity could be reduced (by epinephrine for example), the rate and efficiency of contraction would be increased and the loss of tension and energy waste during systole would be reduced The frictional energy loss due to internal viscosity accounts for increased heat production in muscles which shorten during contraction

RAPID STRETCH OF RELAXED MYOCARDIAL BUNDLES A very small force will gradually elongate relaxed myocardium to considerable lengths On the other hand the myocardium resists any rapid change in length because of internal viscosity In other words a rapid stretch is opposed by a prompt and significant rise in tension of the fibers (Fig 6) In an intact heart an abrupt inflow of blood would be opposed by this increased resistance to stretch while a slower inflow might induce greater distention with less filling pressure

If viscosity in myocardial fibers is a prominent feature in the intact mammalian heart, a series of intriguing postulates can be evolved Intraventricular pressure rises rapidly during the isometric period of contraction because the myocardial bundles need not shorten significantly As soon as ventricular ejection begins the myocardial fibers begin to shorten and their tension falls off partly because of internal friction or viscosity effects The intraventricular pressure falls off correspondingly and the rate of systolic ejection slows during the latter part of systole Since viscosity is high in myocardial bundles their tension drops to very low levels immediately after contraction stops so that early diastolic filling meets little opposition However if the inflow is rapid the ventricular myocardium is rapidly stretched so that tension is increased and further distention is resisted If this is true a rapid diastolic filling should stop abruptly in early diastole while a slow inflow should produce progressive filling during the entire diastolic interval It was previously noted that when epinephrine produces more rapid ventricular ejection myocardial shortening is more extensive and according to Opdyke[13] diastolic filling is more rapid Since the amount of energy lost through friction caused by myocardial viscosity depends upon the rate and extent of the change in fiber length all of these factors involve either greater energy waste or less viscosity In other words epinephrine must either increase the energy release by the contractile mechanism to overcome increased viscosity or reduce the energy loss by diminishing viscosity

These hypotheses are interesting points of departure for speculation but cannot be accepted without additional evidence However one point is clear The efficiency of myocardial contraction would be materially improved by any mechanism which reduced the rate and extent of myocardial shortening The contractile tension would be more effectively maintained and the frictional energy loss would be diminished as the degree of myocardial shortening is lessened even though stroke volume and energy release remain constant

The Relation of Diastolic Volume to the Degree of Myocardial Shortening

The extent of myocardial shortening can be reduced without changing the stroke volume if the diastolic distention of the ventricles is increased Consider a thin-walled elastic sphere with a radius of 10 cm a circumference of 62 8 cm and a volume of 4186 cc If the radius and circumference were uniformly reduced by one-half (radius 5 cm and circumference 31 4 cm) the volume would be reduced to 523 cc. In other words to reduce the circumference of a sphere by one half nearly 90 per cent of its volume must be removed Doubling the radius (20 cm) would increase the volume to nearly 33 500 cc Thus a very slight reduction in circumference of a large sphere would eject a very much greater volume than the same reduction in circumference of a small sphere Superficial spiral muscles tend

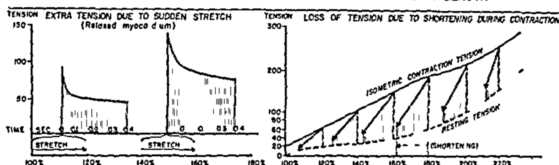


FIGURE 6 With the recording technique illustrated in Figure 5 relaxed muscle was found to respond to a rapid stretch by a prompt increase in tension which diminished progressively as the muscle remained elongated This illustrates the viscous property of muscle by which it exerts tension to resist rapid elongation Although myocardium rapidly develops and sustains high tension during isometric contraction the contractile tension drops precipitously if myocardium is permitted to shorten by 20 per cent of resting length during contraction as indicated by the diagonal arrows The viscosity of muscle is therefore expressed as a loss of contractile tension during rapid shortening (after Lundin[15]) Since blood cannot be ejected from the chamber without shortening of the fibers, viscosity must have an important bearing on the quantity of blood which a chamber can eject

under *isometric* conditions has been studied by a number of investigators Using a condensor myograph, Lundin[15] studied the tension produced during myocardial contraction with and without shortening of the muscle and under many other conditions

Isometric Contraction When a strip of myocardium is stimulated to contract without allowing it to shorten, tension develops very rapidly and is well sustained during the period of contraction Lundin[15] found that tension developed during the contraction is related to the length of the fiber, as indicated in Figure 5, which corresponds to the length-tension diagram of Frank (Fig 2, Chapter 6) *To obtain this* graph, Lundin gradually stretched a bundle of myocardium until it just began to exert tension while relaxed This was considered the resting length (100 per cent in Fig 5) Additional stretch applied to the relaxed fiber progressively increased resting tension Contraction of the myocardium at various degrees of stretch produced increased tension *superimposed* on the resting tension The maximum tension produced by contraction occurred when the myocardium was about 180 per cent of the resting length " Changes in ' distensibility ' and ' contractility " would require that this graph be *modified as indicated* in Figure 11*A* An isometric contraction occurs in the course of normal systole in intact hearts During the period of isometric contraction the intraventricular pressure rises rapidly, but no blood is ejected from the ventricular chambers Without myocardial shortening, no blood is *pumped and no useful work is accomplished* The tension of contracting myocardial fibers during changes in length is vitally important, but has received little attention

Myocardial Viscosity during Contraction When a bundle of myocardium is allowed to shorten after the onset of contraction, the tension produced by isometric contraction falls precipitously (Fig 6) This *phenomenon has been related to high internal* "viscosity" of myocardial fibers ' Viscosity" in this sense refers to the sharp rise in internal resistance or friction in a substance during sudden movement For example, molasses will flow slowly in response to a small force, but a tremendous force is required to produce rapid acceleration If a contracting muscle shortens abruptly, a portion of the energy of contraction is utilized to overcome the high resistance to sudden change in length of the muscle fibers Similar viscosity effects in skeletal muscle have been described by *Gasser and Hill,*[16] *Buchthal et al*[17] and many others The high viscosity of myo-

tion generally corresponds to a reduction in the chamber from volume I to volume II in Figure 7 Although the same stroke volume can be ejected by a change from volume II to volume III (Fig 7) the relative degree of myocardial shortening would be much greater When the diastolic volume is large a relatively large stroke volume can be ejected with small degrees of myocardial shortening As the degree of myocardial shortening decreases the tension is more effectively maintained during ejection the loss of energy due to viscosity or internal friction is diminished and the efficiency of the contractile mechanism is improved i e more work is accomplished per unit of oxygen consumed In contrast more complete systolic ejection requires greater energy release because of greater energy loss—in short increased contractility '

Since the free wall of the right ventricle corresponds to a segment of a large sphere

THE DEGREE OF MYOCARDIAL SHORTENING IN THE VENTRICULAR WALLS

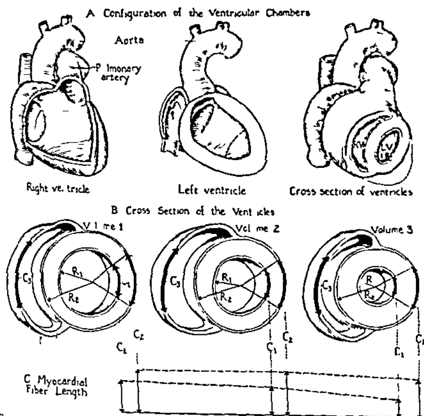


FIGURE 8 The right ventricular cavity is enclosed by the convex interventricular septum and the concave free wall, which may be considered a segment of a very large sphere Very slight shortening of the fibers in the free wall of the right ventricle (C_3) will eject very large volumes (see Fig 7)

The left ventricle has been compared to a very thick-walled cylinder with a conoid segment at the apex (see Chapter 1) The circumferentially arranged deep constrictor fibers account for most of the wall thickness which encloses the cylindrical portion of the chamber The deep constrictor fibers form a cuff of muscle which is so thick that the circles described by the inner layers have a much smaller radius (R_1) and circumference (C_1) than those described by the outer layers (R_2 and C_2) As the left ventricle contracts the inner layers must shorten to a greater degree than the outer layers in ejecting a particular volume On the basis of this analysis during any normal systolic ejection the outer layers of the deep constrictor muscle must shorten to a lesser extent and the superficial spiral muscles shorten least of all It is possible that no two layers of myocardial fibers shorten to exactly the same extent during ejection

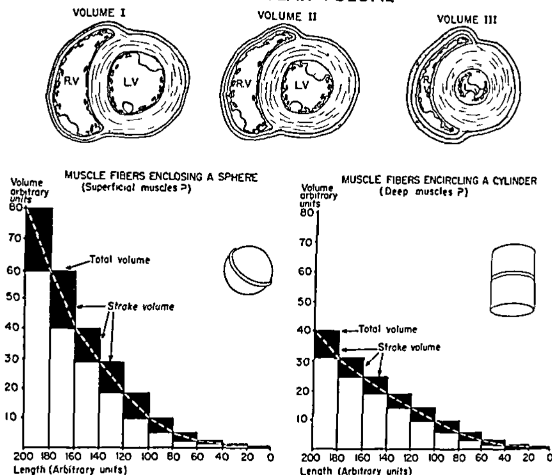


FIGURE 7 The volume of blood ejected by a ventricle (stroke volume) depends upon two factors (*a*) the diastolic volume and (*b*) the amount of myocardial shortening Normally the ventricles are well distended with blood during diastole (volume I) and eject only a portion of the blood within the chambers during systole (volume II) Similar volumes of blood could theoretically be ejected from less distended ventricles (such as volume II) by much more complete systolic emptying (volume III)

The superficial spiral muscles encircle a large volume which is roughly spherical in shape Under these conditions very slight degrees of myocardial shortening will eject very large volumes The larger the initial volume the greater the volume ejected for a particular degree of myocardial shortening as indicated by the black areas on the left.

The deep constrictor muscles encircle the cylindrical portion of the left ventricular chamber The change in volume produced by a reduction in the circumference of a cylinder is much smaller (black areas on the right) than is produced by the same reduction in circumference of a sphere (black areas on the left) Furthermore the circumference of the left ventricle is much smaller than the circumference of the entire heart Thus the superficial spiral layers of myocardial fibers have a much greater initial length and enclose a sphere so very slight shortening ejects large volumes The deep constrictor muscles describe circles of small circumference around a cylinder so they must shorten a great deal more to eject the same volume

to conform most closely to a spherical shape, and this analysis applies within limits to these myocardial fibers

The deep constrictor muscles in the left ventricle are generally arranged circumferentially around a roughly cylindrical cavity Here again, the reduction in volume produced by a reduction in circumference is much greater when the original circumference is large than when the initial circumference is small Thus, the degree of myocardial shortening required to eject a particular stroke volume is much less if the initial fiber length (diastolic volume) is great Evidence has been presented that under normal conditions, ventricular contrac-

must stretch the connections between them In other words, part of the tension developed by the contracting myocardial fibers must be expended in applying tension to the interfascicular connections This interfascicular tension represents wasted energy so far as ventricular ejection is concerned because it actually opposes movements of the ventricular walls However, as the ventricles relax, the potential energy stored as interfascicular tension is released tending to restore the ventricular cavities toward their diastolic dimensions and facilitating rapid ventricular filling during early diastole

In some respects the contractile energy which is stored as interfascicular tension has functional significance similar to that of myocardial viscosity For example, the amount of energy stored as interfascicular tension probably increases as systolic ejection becomes more complete and decreases as the ventricles function at large diastolic and systolic dimensions The ventricular volume at which the interfascicular tension is minimal has not been definitely established As the ventricles relax the interfascicular tension should tend to restore the ventricles to that particular ventricular volume However, the effective filling pressure could distend the ventricles beyond the level of minimal interfascicular tension by distorting the interfascicular connections in the opposite direction In all probability, the ventricular volume at which the interfascicular tension is minimal is reached at some point during diastole The functional significance of interfascicular tension during diastolic filling will be considered in a subsequent section

The relation of myocardial viscosity and interfascicular tension to Starling's law of the heart The basic principle that the energy released by contracting myocardial fibers is proportional to their initial length (diastolic volume) has generally been regarded as a fundamental property of the contractile mechanisms which it probably is In addition the contractile energy wasted to overcome myocardial viscosity and create interfascicular tension is diminished when the ventricles function at large diastolic and systolic dimensions Thus not only is more

TENSION DEVELOPED BETWEEN MYOCARDIAL LAYERS (INTERFASCICULAR TENSION)

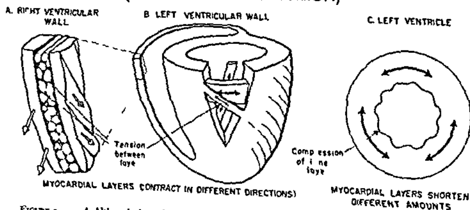


FIGURE 9 *A* Although the right ventricular wall is quite thin, it contains myocardial fibers oriented in three different directions Simultaneous contraction of these fibers must create tension in the fibrous and myocardial connections between the different layers (interfascicular tension)

B The left ventricular wall is also composed of at least three layers of muscle oriented primarily in three different directions (see Chapter 1) Interfascicular tension must develop in the connections between these layers during contraction.

C The different layers of the thick walled left ventricles must contract to different degrees in ejecting a particular volume of blood (see Fig 8) This presumably causes tensions between layers of circularly arranged fibers as well as compressing the inner layers

while the left ventricle resembles a cylinder, equal *myocardial* shortening in the two chambers would produce much larger stroke volumes from the right ventricle than from the left The right and left ventricles must eject roughly equal quantities, so the degree of myocardial shortening cannot be equal in the two ventricles

THE DEGREE OF MYOCARDIAL SHORTENING IN DIFFERENT MUSCLES OF THE HEART The various myocardial bundles in the ventricles are oriented in different directions and describe circles of different diameters, so the degree of myocardial shortening must vary widely *in different layers* In Figure 8*B*, the relative wall thickness and the diameter of the left ventricular chamber at a particular size are represented by volume I Volume II represents the same cross section with the ventricular volume reduced by *half* *In both cases it is obvious that the* radius and circumference of the inner layer of myocardium (R_1 and C_1) are less than those of the outer layer (R_2, C_2) During contraction from volume I to volume II, the radius and circumference of the inner layer are reduced much more than those of the outer layers This means that the inner layer of myocardium must shorten more than the outer layers If this analysis is correct, the thickness of the ventricular walls should increase during systole and *decrease during diastole In the cinefluorographic* angiocardiogram shown in Figure 13, Chapter 1, such an increase in wall thickness during systole can be visualized

It is apparent that during any particular ventricular contraction, *the inner layers of* the deep constrictor muscles shorten to the greatest extent Outer layers of the deep constrictor fibers shorten less and the superficial spiral muscles shorten the least The relative degree of myocardial shortening *in the inner* lining of spiral muscle (trabeculae carneae) and papillary muscles cannot be assessed by this type of analysis The difference in degrees of shortening by various myocardial layers is diminished when the diastolic and systolic volumes remain large, the maximum difference between the shortening of the superficial spiral muscle and that of the inner layer of deep constrictor fibers would occur when the left ventricle *empties maximally* (see volume III in Fig 7)

FACTORS OPPOSING COMPLETE VENTRICULAR EMPTYING Muscle fibers cannot shorten to an infinitely small length The maximum degree of myocardial shortening probably ranges around 30 per cent of the resting length, but it is impossible to determine at what size of an intact ventricle the myocardial fibers are at resting length If all the myocardial fibers constricted 30 per cent of their initial length, the inner layer of circumferential fibers would have attained this value and ceased contributing any tension, while the outer layers and particularly the spiral muscles might be able to contract still more From this point on *further shortening by the outer layers would* require an expenditure of energy in wrinkling and deforming the inner layers

The trabeculae carneae represent preformed wrinkles and combine with the capillary muscles to occupy space in the ventricles This permits more complete systolic ejection than would be possible if the inner walls of the ventricular chamber were smooth (see Fig 7) Because of the space occupied by papillary muscles and trabeculae carneae, even the inner layers of circumferential fibers in the left ventricle can describe circles of reasonable diameter when the left ventricle is virtually emptied This mechanism is less important in the right ventricle because of (*a*) its thin wall (*b*) *the very long fibers* which enclose the cavity and (*c*) the large circles described by these fibers

Interfascicular tension The myocardial bundles in the different muscle layers of the ventricular walls *are oriented* in different directions (Fig 9) Furthermore, the fibers must shorten to different degrees during their contraction But these layers are bound tightly together During ventricular con*traction, the relative movements* and displacements of these different muscle layers

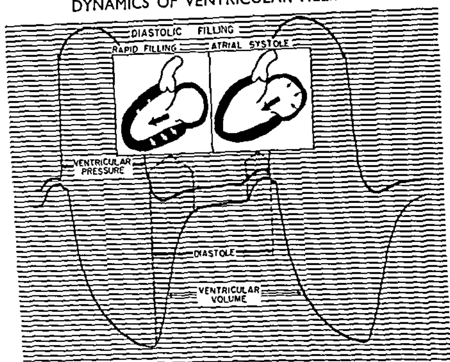


FIGURE 10 The diastolic interval is composed of three portions (a) In early diastole ventricular filling is extremely rapid, which indicates very great distensibility of the ventricles Indeed the filling pressure is often minimal at this stage when blood is surging into the ventricles This is probably due primarily to the release of interfascicular tension facilitated by the pressure gradient from atrium to ventricle (b) In mid-diastole, ventricular filling is slowed or stopped depending again upon the relation between filling pressure and ventricular distensibility (c) During atrial contraction an additional increment of blood surges into the ventricular chambers the magnitude of which depends upon the vigor of atrial contraction the increase in ventricular pressure and the distensibility of the ventricular walls

fascicular tension is being released tending to restore the ventricular chambers toward their diastolic dimension The resistance to distention at this stage is so slight that a rush of blood enters the ventricle Indeed the pressure in the atria and ventricles often drops to its lowest level early in diastole A drop in pressure during the most rapid ventricular filling indicates that the ventricle is expanding faster than the blood flows into the chamber This extremely great distensibility of the ventricles is most logically explained by the released interfascicular tension

The process described above is distinctly reminiscent of a theory which has recurred through the years that the ventricles sucked blood into the chambers during diastole As recently as 1952 Burch et al[18] analyzed pressure and volume curves and demonstrated that ventricular filling proceeded while intraventricular pressure diminished and labeled this phenomenon a suction effect (see Fig 8 Chapter 6)

DIASTASIS At the end of the rapid filling phase the intraventricular pressure frequently levels off and remains fairly constant until the succeeding atrial contraction During this interval the forces tending to distend the ventricles become balanced by the factors which oppose further distention and ventricular volume either remains constant or increases gradually There is considerable variability in the rate of filling during the period of diastasis

PRESYSTOLIC FILLING Just preceding each normal ventricular contraction the atrium contracts in response to a wave of

energy released when the ventricles contract from larger ventricular volumes, but less is wasted, so the net useful energy is disproportionately greater

Clearly, the ventricles function more efficiently at large diastolic and systolic dimensions because of three factors: (a) Starling's law of the heart, (b) myocardial viscosity, and (c) interfascicular tension On the other hand, in accordance with the law of Laplace (see Fig 11), myocardial fibers must develop higher tension to produce a particular level of intraventricular pressure when myocardial fibers describe circles with larger radii

The law of Laplace According to the Laplace formula ($P = T/R$), the pressure (P) developed by a particular level of wall tension (T) is inversely proportional to the radius of the chamber This law was invoked to explain the difference between the wall thicknesses of the aorta and the systemic capillaries when these widely different structures sustain pressures of the same order of magnitude (see Fig 8, Chapter 2)

Applied to the contracting ventricle, the law of Laplace indicates that the myocardial tension required to sustain a particular level of intraventricular pressure diminishes as the radius of the chamber is reduced by ejection In other words, this factor would tend to compensate to some extent for the loss of myocardial tension through myocardial viscosity and interfascicular tension On the other hand, if the diastolic volume is increased, greater myocardial tension is needed to develop a particular level of intraventricular pressure This factor may explain the development of hypertrophy rather than dilation when the left ventricle is exposed to chronic pressure loads (see Chapter 8)

Factors Affecting the Degree of Ventricular Emptying

During isometric contraction, intraventricular pressure rises abruptly until it exceeds the pressure in the corresponding arterial trunk The intraventricular pressure is determined at any instant by the myocardial tension and the effective radius of the circles described by the myocardial fibers As soon as intraventricular pressure exceeds the corresponding arterial pressure, blood is ejected from the chamber as the myocardial fibers begin to shorten The myocardial tension falls because of myocardial viscosity A portion of the myocardial tension is diverted to produce interfascicular tension Thus, during the later part of systole, the rate of ejection slows although the intraventricular pressure remains high Ejection of blood from the ventricles continues only so long as the myocardial fibers continue to sustain adequate tension while they are shortening In other words, the volume of blood ejected during a ventricular contraction is determined by the amount of myocardial shortening which occurs before the net tension of the fibers drops below that required to maintain an interventricular pressure greater than that in the corresponding artery The volume of blood ejected per stroke can be increased in two ways (a) greater myocardial contractility, which implies an increase in the degree of myocardial shortening per unit of arterial pressure, and (b) greater diastolic distention

Dynamics of Ventricular Filling

When the heart is beating at a slow rate, diastolic filling occurs in three phases (1) At the onset of diastole, the ventricles begin to distend at a more rapid rate than that at which systolic ejection emptied them (Fig 10) (2) After the rapid filling phase, ventricular volume increases slowly or remains constant (3) During the auricular contraction an additional increment of blood enters the ventricle immediately preceding the next ventricular systole With tachycardia the shortened diastolic interval encroaches upon the period of diastasis until it ultimately disappears In this case auricular contraction occurs during or immediately following the rapid filling phase

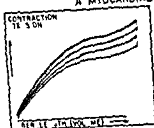
THE RAPID FILLING PHASE At the very beginning of ventricular filling the inter

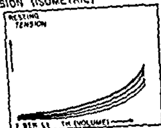
FACTORS AFFECTING SYSTOLIC EJECTION AND DIASTOLIC FILLING

FACTORS AFFECTING STROKE VOLUME

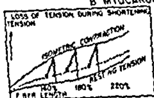
SYSTOLIC EJECTION | DIASTOLIC FILLING

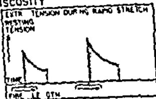
A MYOCARDIAL TENSION (ISOMETRIC)



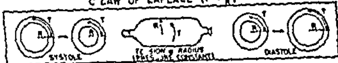


B MYOCARDIAL VISCOSITY

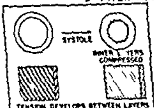




C LAW OF LAPLACE (P ∝ T/R)



D INTERFASCICULAR TENSION



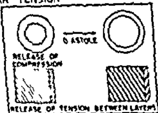


FIGURE 11 Factors which affect stroke volume are summarized schematically The effects of each factor on the degree of systolic ejection appear in the left column and on the extent of diastolic filling in the right

A Myocardial tension during systole is affected by initial fiber length, according to Starling's experiments However the magnitude of the contractile tension also depends upon the "condition of the *myocardium*" as affected by coronary oxygen supply epinephrine acetylcholine and autonomic stimulation and many other conditions This fact is illustrated by a family of curves rather than by a single curve in accordance with results of Sarnoff and his colleagues (see Chap 6) The extent of diastolic filling is *determined* by the length-tension relations of the relaxed myocardium as *influenced* by changes in "distensibility of the *myocardium*." These graphs indicate the length-tension relations under isometric *conditions* when no blood would be ejected from the ventricle When myocardial shortening occurs additional factors come into play

B Because of viscosity effects the myocardium tends to resist any sudden change in length If the fibers shorten rapidly during contraction the contractile *tension* is rapidly diminished presumably by *internal friction* within the fibers For this reason *contractile tension* is best maintained with *minimal* myocardial shortening during ejection of a particular stroke volume as occurs at large diastolic and systolic volumes The myocardium also resists a sudden elongation which may be a factor in the abrupt transition between *early rapid* filling and slow mid-diastolic filling

C According to the law of Laplace greater contractile tension is required to sustain a given ventricular pressure as the radius of the fibers is *increased* Thus the advantages gained by beginning contraction at great initial lengths must be balanced against the greater myocardial tension required to develop high ventricular pressures The tension in the relaxed myocardial fibers must be progressively greater for the same filling pressure as diastolic distention progresses This factor facilitates *diastolic* filling

D During systole tensions developed *between* layers of myocardial fibers contracting *in different* directions and to different degrees Energy diverted to interfascicular tension is lost as far as ejection of blood is concerned and becomes greater as the degree of myocardial shortening increases During *diastole* the release of the interfascicular tension and of the *compression* of inner layers tends to restore the ventricle toward its diastolic size and probably *contributes* greatly to the *very rapid* ventricular filling which occurs during early diastole

excitation spreading through the atrial walls As the atrial contraction reduces the capacity of the atrial chamber, a corresponding quantity of blood is displaced Since there are no effective valves between the atria and the corresponding great veins and the A-V valves are open, atrial blood may be forced either into the ventricular chambers or in a retrograde direction into the great veins Judging from cinefluorographic observations, blood in the right atrium may follow either one or both of these courses, under varying conditions Generally, the supplementary filling during atrial systole may range around 30 per cent of the total, but may drop to 8 per cent during vagal stimulation or rise to 44 per cent in response to epinephrine[12]

Cannon et al[19] have reported that increases in ventricular diastolic size correlate with reduction in atrial size Atrial contraction is probably an important mechanism for controlling cardiac output by influencing the degree of ventricular filling The increased presystolic ventricular filling following epinephrine administration could be attributed to a number of factors, including increased vigor of atrial contraction (e g , increased atrial contractility), increased ventricular distensibility, reduced distensibility of the veins preventing retrograde flow, and possibly many others

SUMMARY

For many years, the control of stroke volume has been explained largely on the basis of two fundamental concepts (*a*) The diastolic volume of the ventricles is determined by the effective filling pressure, and (*b*) the energy released by the contracting myocardium is proportional to the initial length (diastolic volume) of the ventricular musculature (Starling's law of the heart) Evidence is accumulating that the ventricular volume can vary without corresponding changes in effective filling pressure through changes in "distensibility" of the ventricles When considering the basic nature of the contractile process, the close functional relation of the myocardium to smooth muscle, the response of myocardial strips to sudden changes in length, the effects of epinephrine on the resistance to distention, and the rate of distention no facts were uncovered which indicate that this possibility can be excluded On the contrary, available evidence makes a fairly strong case for the occurrence of both changes in distensibility and changes in contractility under the influence of autonomic control and circulating hormones such as epinephrine An increase in contractility is evidenced by a greater energy release without an increase in ventricular filling pressure or diastolic volume Under normal conditions the ventricles function at relatively large diastolic and systolic dimensions, so an increase in stroke volume can be attained by an increase in the degree of systolic emptying, by an increase in the extent of diastolic filling or by a combination of the two Increased systolic ejection implies an increase in contractility, and appears to play a significant role in the cardiac adjustment to exertion in intact, unanesthetized dogs The heart rate also plays an important role in the stroke volume, and in the ventricular volume and cardiac output If heart rate, diastolic volume, and systolic ejection are under the influence of autonomic reflexes, cardiovascular responses can be promptly adjusted to varying circulatory demands through direct influence on the cardiac musculature as well as through peripheral vascular mechanisms As a working hypothesis it is proposed that certain factors which tend to produce an increase in heart rate also may act simultaneously to augment stroke volume, so that the effective filling pressure is maintained at relatively low levels unless the cardiac output fails to meet the circulatory demands In this case, diastolic filling may be further increased by an augmented filling pressure (increased central venous pressure)

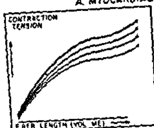
The neural and humoral controlling mechanisms act by changing the functional characteristics of the myocardium (con-

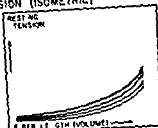
FACTORS AFFECTING SYSTOLIC EJECTION AND DIASTOLIC FILLING

FACTORS AFFECTING STROKE VOLUME

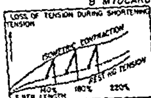
SYSTOLIC EJECTION DIASTOLIC FILLING

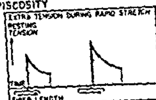
A MYOCARDIAL TENSION (ISOMETRIC)



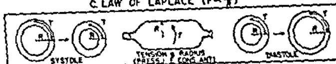


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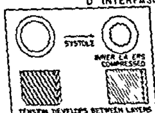




C LAW OF LAPLACE $(P \propto \frac{T}{R})$



D INTERFASCICULAR TENSION



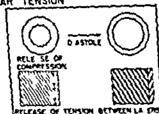


FIGURE 31 Factors which affect stroke volume are summarized schematically The effects of each factor on the degree of systolic ejection appear in the left column and on the extent of diastolic filling in the right

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tractility and distensibility) The diastolic volume and degree of systolic ejection are also affected by physical, geometric and architectural factors described in relation to myocardial viscosity, the Laplace relation and interfascicular tension The effects of these mechanisms on ventricular function are summarized in Figure 11 For additional details the reader is referred to previous publications of the author [20, 21] A more complete explanation of normal cardiac function and the responses of the heart to various disease processes results from a consideration of all these factors The application of these concepts to routine cardiac diagnosis is a major objective in the succeeding chapters

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Part Three

CONGESTIVE HEART FAILURE

Introduction to Part Three

Most forms of heart disease ultimately reduce the maximum quantity of blood which the ventricles can pump through the vascular system per minute Impairment of cardiac performance may not produce either signs or symptoms for long periods of time because of various compensatory mechanisms and different types of reserve capacity Evidence of subnormal cardiac function is gen*erally related to the depletion of the various* forms of cardiovascular reserve which are described in Chapter 8

The advanced stages of many different pathologic conditions in the heart are accompanied by typical changes in the vascular system upstream from the affected ventricular chamber Thus, left ventricular failure produces abnormalities in the pulmonary vascular bed which are expressed primarily as deranged respiratory function Right ventricular failure produces congestion in the systemic venous system and peripheral edema The pathologic physiology of the cardiovascular system which accounts for the typical signs and symptoms of congestive heart failure is discussed in Chapter 9

The discussion of congestive heart failure precedes methods of cardiac diagnosis for *three reasons (a) the major manifestations* of this condition result from changes in the peripheral vascular systems, (*b*) the resulting signs and symptoms are not elicited by methods for cardiac diagnosis and (*c*) recognition of classic pictures of congestive failure does not require extensive training because intelligent laymen often correctly interpret them

Chapter 8

The Cardiac Reserve

The cardiovascular system is designed to meet the widely varying metabolic requirements of the body, shifting blood flow patterns to favor one set of tissues or another as they serve various bodily activities However, the total sustained blood flow through the system is limited Even a normal person cannot run at his maximum speed on a hot day after a heavy meal because such action would demand simultaneous increases in blood flow through the muscles splanchnic bed and skin When an individual develops heart disease, the maximal cardiac output he can sustain is usually curtailed the reserve capacity of the cardiovascular system being utilized to make up the deficit imposed by disease during routine activity Thus the attributes of the various components of the cardiovascular reserve are very important in understanding the functional response to heart disease

The cardiac reserve will be considered in terms of seven factors (*a*) the venous oxygen reserve (*b*) the maximum effective heart rate (*c*) the systolic reserve volume (*d*) the diastolic reserve volume (*e*) the work of the heart, (*f*) the coronary vascular reserve and (*g*) cardiac enlargement. Particular attention will be directed to the limitations in each factor

THE VENOUS OXYGEN RESERVE

It was pointed out in Chapter 5 that delivery of oxygen from the blood to the tissues depends upon a diffusion gradient determined by the differences in the partial pressures of oxygen in the blood and in the cell If the cells become more active and take up oxygen at a more rapid rate the lower end of this diffusion gradient will fall, the transfer of oxygen to the cells will be accelerated and a greater proportion of the oxygen will be removed from the blood (Fig 2 Chapter 5) Other conditions being the same, the oxygen remaining in the venous blood after it has passed through the capillaries represents a reservoir which can be utilized if the metabolic activity accelerates (Figs 2, 3 Chapter 5)

The Arteriovenous Oxygen Difference

Each 100 cc of arterial blood entering the capillary networks contains approximately 19 cc of O_2 Different tissues extract different amounts of oxygen from the capillary blood The amount of oxygen extracted from each increment of blood during its passage through the capillary networks is determined by the relation between the oxygen consumption of a particular tissue *and the volume* flow of blood

The oxygen consumption and blood flow in cerebral vessels is normally quite constant, so the oxygen extraction remains relatively fixed The blood flow through the kidneys skin and inactive muscle is so great in relation to oxygen consumption that large quantities of oxygen remain in the venous blood leaving these tissues Indeed, most inactive tissues extract relatively little of the oxygen available in the arterial blood In contrast, active skeletal muscle and the myocardium extract more than 75 per cent of the oxygen from the capillary blood Vasoconstriction in inactive tissues would tend to shunt blood through the dilated capillary networks in the active muscles During muscular exertion blood flow may be diverted into active muscles from the skin, kidneys gastrointestinal tract spleen etc. These tissues then utilize more oxygen from the remaining

THE UTILIZATION OF VENOUS OXYGEN RESERVE

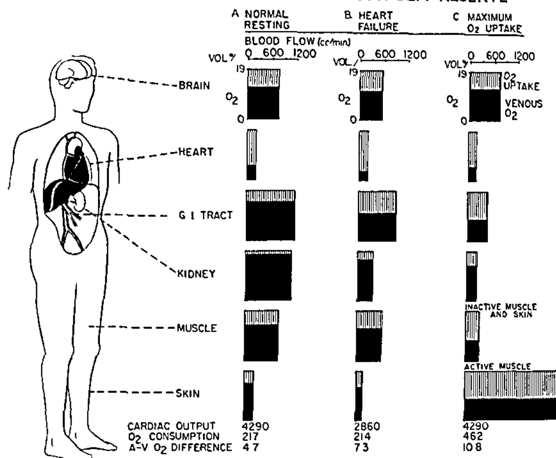


FIGURE 1 The rectangular area delimited by plotting oxygen content against blood flow represents the quantity of oxygen per minute delivered to each tissue by the arterial blood The area covered by vertical lines indicates the quantity of oxygen extracted by each tissue The black areas represent the venous oxygen reserve *the quantity of oxygen remaining in the blood when it leaves the tissue*

A The normal distribution of blood flow and oxygen extraction is the same as in Figure 3 Chapter 5

B In patients with advanced congestive heart failure the resting cardiac output may be abnormally low (2860 cc per minute) A greater proportion of the venous oxygen reserve is utilized because flow is diminished *and greater oxygen extraction occurs in all the tissues except the myocardium Even cerebral blood flow is* diminished

C A normal individual with an average resting cardiac output (4290 cc per minute) could theoretically double his oxygen consumption by maximal utilization of the venous oxygen reserve Assuming that the cere*bral and coronary flow remain normal the oxygen extraction from the blood in the splanchnic bed skin* and inactive muscle could be increased to about 12 volumes per cent and in the kidney to 5 5 volumes per cent These are the maximal arteriovenous oxygen differences reported in the literature If blood flow is conserved by this means one half of the cardiac output can be diverted to active muscles greatly augmenting their *supply of oxygen without an increase in cardiac output Neither the normal individual nor the patient* with acquired heart disease utilizes venous oxygen reserve to this extent (Data compiled from the literature [6] and organized in this form by Dr Loren D Carlson University of Washington)

blood flow at the expense of a moderate reduction in the oxygen tensions within the tissues Thus, increased oxygen consumption characteristically causes an increased arteriovenous oxygen difference in both active and inactive tissues In normal subjects an increase *in oxygen consumption* by 100 per cent produces an average increase in cardiac output of only about 70 per cent [1] The difference between these values is made up by increased extraction of oxygen from the blood and a widened arteriovenous oxygen difference

Oxygen Extraction in Patients with Heart Failure

As cardiac function is impaired by disease, the maximum sustained increase in

cardiac output is curtailed Under these conditions increased oxygen needs are met by a more complete oxygen extraction than normal In patients with seriously limited cardiac performance the resting cardiac output may be significantly diminished even though the oxygen uptake remains normal For example a normal resting subject with a mean cardiac output of 4.90 cc per minute and an oxygen consumption of 217 cc per minute has an average arteriovenous oxygen difference of 4 7 volumes per cent (Fig 1 A) Patients with heart failure have about the same resting oxygen uptake (214 cc per minute) even though the cardiac output is significantly diminished (2860 cc. per minute) but the arteriovenous oxygen difference is increased (7 3 volumes per cent) (Fig 1B) The increased oxygen extraction in the various tissues is accomplished by reduced blood flow through the skin kidney, gastro-intestinal tract skeletal muscle and even through the brain When patients with such advanced heart disease exert themselves even mildly the oxygen consumption increases largely by further reduction in venous oxygen content from various tissues *However a further diminution in blood flow through the cerebral circulation kidneys and splanchnic bed is not well tolerated and unpleasant symptoms discourage any form of physical exertion*

Maximum Oxygen Uptake

A greatly increased oxygen consumption can theoretically be attained solely *through* utilization of the venous reserve oxygen without any increase in cardiac *output* Assuming that blood flow and oxygen extraction in the brain and heart remained normal and that the maximum tolerable oxygen extraction in splanchnic bed skin and muscle was 12 volumes per cent and in the kidney was 5 5 volumes per cent the total oxygen consumption could be doubled without any change in total systemic blood flow (Fig 1C) Note the tremendous potential increase in oxygen delivery to active muscle by more complete utilization of venous oxygen reserve through redistribution of blood flow Neither normal individuals nor patients with advanced heart disease utilize these mechanisms to the fullest extent Such a marked reduction in renal blood flow could probably be tolerated only briefly before it interfered with renal function Indeed such an extreme reduction in renal blood flow is rarely encountered even in patients with advanced congestive failure and extensive edema Reduced renal blood flow resulting from restricted cardiac output may produce serious impairment of kidney function The importance of renal retention of salt and water in congestive heart failure will be considered in Chapter 9

THE MAXIMUM EFFECTIVE HEART RATE

During *sustained* exercise the heart responds to an *increase in volume flow* through the circulation with an *acceleration of the* heart rate, tachycardia Tachycardia encroaches mainly upon the interval of diastasis during which little or no filling occurs (see Fig 2) The maximal effective increase in heart rate is approximately two and a half times (i e , from a resting rate of about 70 beats per minute to levels of 170 to 180 beats per minute) [7] At faster heart rates the rapid filling period is curtailed and stroke volume tends to diminish Tachycardia is very effective in rapidly increasing cardiac output in response to increased systemic blood flow but it involves a sacrifice of efficiency in both ventricular contraction and the diastolic filling Further an increase in cardiac output by extreme tachycardia interferes with coronary blood flow (*vide infra*)

STROKE VOLUME RESERVE

In most normal individuals the stroke volume can be increased from about 70 cc to 180 cc Combined utilization of increased heart rate (2 5 times) and increased stroke volume (2 5 times) increases cardiac output slightly more than six times (Fig 2) The

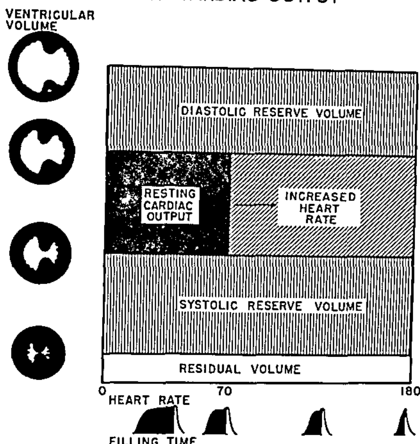


FIGURE 2 The normal resting cardiac output about 5 l per minute (dark stippled area) is the product of stroke volume (about 70 cc) and heart rate (about 70 beats per minute) The cardiac output can increase maximally to about six times the resting value (total cross hatched area) if heart rate and stroke volume increase simultaneously Heart rate can increase to about 180 beats per minute which would increase cardiac output two and a half times if the reduced filling time did not diminish stroke volume Stroke volume can also increase about two and a half times through utilization of the systolic reserve and diastolic reserve volumes The residual volume is the quantity of blood remaining in the ventricle after a maximal systolic ejection.

stroke volume can be increased by either more complete emptying (systolic reserve) or by augmented filling (diastolic reserve)

The Systolic Reserve Volume

At the end of a normal systolic ejection, considerable quantities of blood remain within the chambers (see Chapter 1) A number of interdependent variables discussed in Chapter 7, limit the degree of systolic ventricular emptying Attainment of increased stroke volume by utilization of the systolic reserve volume ordinarily implies an increased "contractility" of the myocardium "Contractility is defined here as the degree of myocardial shortening per unit of outflow pressure (arterial blood pressure) Heart failure appears to result from a loss of myocardial contractility

The Diastolic Reserve Volume

The magnitude of the diastolic filling is determined by the effective filling pressure in relation to the resistance to distention offered by the ventricular walls (Chapters 6, 7) Ventricular contraction beginning at a large diastolic size is favorably influenced by (1) a greater energy release (Starling s law), (2) the large volume of blood ejected per unit of myocardial shortening and (3) reduced internal friction (viscosity) within the myocardium On the other hand, the radius of the circles described by the myocardial fibers is increased and much greater myo-

cardial tension is required to produce equivalent elevation of intraventricular pressure during ejection (according to the formula $P = T/R$) (The factors which determine the extent of diastolic distention have been discussed in detail in Chapter 7) The heart appears to function with greater efficiency at larger diastolic (and systolic) size However the question of efficiency mu t be considered in terms of the quantity of useful work performed in relation to the quantity of fuel consumed by the myocardium (oxygen utilization)

THE WORK OF THE HEART

Energy produced by the oxidation of organic fuels such as glucose glycogen or lactic acid is partly converted to mechanical energy during myocardial contraction For purposes of discussion the avenues of energy dissipation will be divided into two main categories (1) useful work, expressed as the energy expended for ejection of blood under pressure into the arterial trunks and (2) wasted energy including all other avenues of energy dissipation

Useful Work of the Heart

The useful work of the heart occurs during active ejection of blood from the ventricular chambers No work is accomplished during isometric contraction isometric relaxation or diastole During the ejection phase of ventricular contraction blood is propelled into the root of the aorta A major portion of the potential energy is stored as tension in the arterial walls According to Prec et al [8] the potential energy developed by the left ventricle is more than 98 per cent of the total useful work kinetic energy amounts to only about 0.25 to 2 0 per cent Since the stroke volume and velocity of flow for the two ventricles are approximately equal equal quantities of kinetic energy are transferred to the blood by the two ventricles The kinetic energy is a greater proportion of the total useful work of the right ventricle (about 2 4 to 1. 5 per cent) because the potential energy is much less than in the left ventricle The distinction between potential and kinetic energy is somewhat artificial because most of the potential energy is converted to kinetic energy in producing flow through the vascular elements In other words the arterial blood pressure produces flow through the circulatory bed so the potential energy is converted into kinetic energy and then into heat due to friction The total quantity of useful work accomplished by the heart is ultimately dissipated by frictional losses as the blood flows through the circulation except for the potential energy at the point of venous inflow into the next ventricle in the circuit. This energy is utilized to distend the ventricle during diastole

Energy Waste During Ventricular Contraction

Energy waste during ventricular contraction takes many forms. The metabolic activity required to maintain and repair the myocardial cells is essential for myocardial integrity but does not contribute to the circulation of the blood The energy expended in the wave of excitation is in a similar category However these two processes dissipate negligible amounts of energy in comparison to other sources of energy waste associated with chemical reactions myocardial viscosity turbulence in the blood or energy stored as interfascicular tension (Chapter 7) A major portion of both useful work and energy waste occurs during ventricular systole, illustrated schematically in Figure 3 As the useful work of the heart increases the amount of energy waste usually increases simultaneously Since the useful work of the heart is the only external evidence of energy dissipation, the large quantities of wasted energy are frequently overlooked although they have considerable functional importance The myocardium must release energy equal to both the 'wasted energy' and the useful work Enough oxygen must be delivered to the heart through coronary blood flow to meet this total energy expenditure Some disease processes interfere with oxygen delivery to

THE TOTAL WORK OF THE HEART

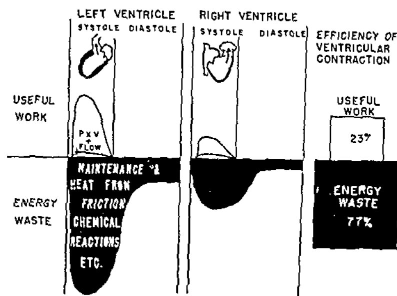


FIGURE 3 The useful work of the heart is the potential and kinetic energy imparted to the blood during the ejection phase of systole The quantity of wasted energy exceeds the useful work by about fourfold and is probably dissipated largely during systole However the exact time relations of this energy waste have never been described The *efficiency of myocardial contraction* $\left(\frac{\text{useful work}}{\text{total energy release}}\right)$ varies widely but averages about 23 per cent [9]

the myocardium (diseases of the coronary arteries, ventricular hypertrophy) Other types of heart disease reduce the efficiency with which the myocardium converts chemical energy into the mechanical energy of contraction

The Efficiency of Ventricular Energy Release

The efficiency of the ventricular myocardium may be defined as the relation of the quantity of useful work performed to the total energy expended The total energy release can be estimated from the oxygen consumption of the myocardium by assuming that 2 kg-m of work are performed in the process of utilizing 1 cc of oxygen Coronary sinus catheterization is providing information on the efficiency of the left ventricular myocardium [9, 11] Measurements of coronary blood flow, myocardial oxygen consumption, and useful work of the left ventricle provide the necessary data for computing the efficiency of the left ventricular myocardium as indicated by the formula

$$\text{Mechanical efficiency (per cent)} = \frac{\text{work of left ventricle (kg-m/min)}}{\text{aerobic energy uptake of left ventricle (kg-m/min)}}$$

The efficiency of the normal left ventricle may improve during exercise when the increase in useful work by the left ventricle is more than the increase in myocardial oxygen consumption On the other hand, in patients with congestive heart failure, the efficiency of left ventricular energy conversion is reduced at rest[9] and declines even further during exercise [12] Cardiac decompensation apparently involves a loss of efficient utilization of glucose (see Chapter 9)

Energy Restoration in the Heart

Since cardiac activity cannot be interrupted for long intervals, the delivery of oxygen and metabolic fuels must be continuously maintained at levels commensurate with the energy released by the myocardium The total energy released during systole must be restored during the succeeding diastolic interval Oxygen and metabolic fuels are delivered to the myocardium

by the coronary blood flow After passing through the capillaries of the coronary system the coronary venous blood of normal humans contains only about 3 9 to 6 9 cc of oxygen per 100 cc of blood (Fig 1) Such complete extraction of oxygen from coronary blood signifies that oxygen tension in the myocardial fibers is very low In other words the myocardium continuously operates in an environment of very low oxygen partial pressure During exercise and other forms of stress the oxygen extraction is even more complete so the oxygen tension immediately around the myocardial cells must be extremely low Since the oxygen extraction from blood in the coronary vessels is so complete the myocardium has little coronary venous oxygen reserve and must depend primarily upon an increase in coronary blood flow to supply increased demands In *this sense the* maximum sustained cardiac *output is* limited by the cardiac efficiency and the coronary blood supply

THE CORONARY CIRCULATION

Anatomy of the Coronary Vessels

The ventricular walls are supplied by three main arterial trunks The left coronary artery arises from the left aortic sinus and divides almost immediately into two branches The anterior descending branch gives off several branches to the anterior septum as it passes along the anterior interventricular groove toward the apex of the heart. The left circumflex branch courses around the base of the left ventricle along the coronary sulcus, and terminates in the posterior descending branch The right coronary artery, originating in the right aortic sinus, reaches the posterior interventricular groove by way of the coronary sulcus at the base of the right ventricle From the coronary ring a number of branches descend to supply the ventricular walls The pattern of distribution is somewhat variable particularly in the posterior aspect of the ventricular walls and septum Schlesinger[13] has described three general patterns of coronary distribution (1) right coronary preponderance, (2) a balanced distribution and (3) left coronary preponderance (see Fig 4) Patients with left coronary preponderance are more apt to succumb to coronary occlusion

Branches from the main coronary vessels descend toward the apex giving off pene-

DISTRIBUTION OF THE CORONARY ARTERIES TO THE VENTRICULAR WALLS

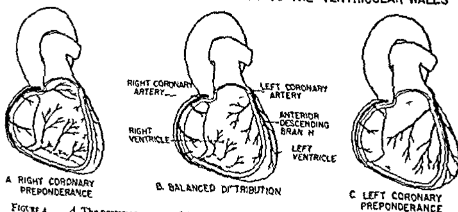


FIGURE 4 *A* The posterior portion of the interventricular septum and part of the posterior aspect of the left ventricle were supplied by the coronary artery in about 48 per cent of a series of postmortem examinations This distribution has been classified as right coronary preponderance

B Balanced coronary distribution occurred in about 34 per cent of specimens

C *Left coronary* preponderance (left coronary *artery* supplying some of the contiguous right ventricle and virtually the entire interventricular septum) occurred in 18 per cent. Patients with left coronary preponderance appear to be more susceptible to coronary occlusions with myocardial infarction. (After Schlesinger M J *Arch. Path.* 30 403-415 1940)

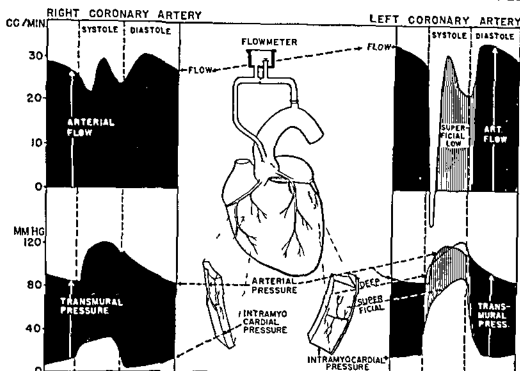


FIGURE 5 The changes in blood flow through coronary arteries during a cardiac cycle are illustrated schematically In the right ventricle the extravascular pressures are smaller than coronary arterial pressure throughout the cardiac cycle (lower black area) and blood flows continuously through the right coronary arteries (upper black area) The extravascular pressures in deep layers of the left ventricular wall probably exceed coronary arterial pressure during most of systole (lower black area) Blood evacuated from the artery surges backward producing retrograde flow in early systole (upper record) Evacuation of blood from the capillaries and veins during systole may facilitate inflow during the subsequent diastole Forward flow through the coronary arteries occurs during the latter part of systole and may represent flow through superficial layers (vertical lines above) where the extravascular pressures are not as high as coronary arterial pressures (vertical lines below) (Compiled from Gregg D E Coronary Circulation in Health and Disease Philadelphia Lea & Febiger 1950)

trating branches which divide into dense anastomotic capillary networks roughly paralleling the courses of the myocardial bundles The myocardial fibers are supplied by capillaries in a ratio of 1 34 1 in the adult heart[14]

Collateral channels connecting the three coronary arterial systems are probably of small caliber Prinzmetal and his associates[15, 16] performed a number of ingenious experiments on normal animals demonstrating anastomotic channels from 70 to 180μ in diameter between the main coronary arterial systems Wiggers[17] marshalled convincing arguments that these collaterals are not normally significant and will not protect the myocardium from abrupt occlusion of its arterial supply He pointed out that flow through collateral channels depends upon the magnitude of the pressure difference between the communicating tubes If the pressures in the various arterial trunks are equal, blood flow through anastomotic connections will be small or absent Gradual establishment of differential pressures associated with progressive occlusion of a main coronary artery may produce differential pressures sufficient to distend collateral channels

Changes in Coronary Blood Flow during the Cardiac Cycle

The volume of blood traversing the coronary circulation is influenced by a number of factors (a) the arteriovenous pressure gradient (the difference between the pressures in the aorta and in the right atrium),

(*b*) the resistance to flow through the coronary vessels as affected by vasomotor control and (*c*) the extravascular pressure Since the coronary vessels travel within the ventricular wall the contracting myocardium compresses them and impedes arterial inflow during the systolic period (Fig 5) According to Gregg and Green[18] coronary flow during diastole is usually greater than systolic flow by more than 2 to 1 (average 2 4 1) When the heart rate accelerates the diastolic intervals are markedly reduced and the coronary blood flow is correspondingly diminished unless dilatation of the vessels supervenes Thus cardiac output is more efficiently augmented by increased stroke volume than by tachycardia on two counts (*a*) greater myocardial efficiency and (*b*) greater total coronary blood flow

Wiggers[19] recently reported evidence indicating that the contractile force of the heart is the chief factor determining coronary flow whether coronary vascular resistance is increased or decreased He emphasized the fact that the peripheral coronary bed fills chiefly during diastole and is compressed during systole The quantity of blood entering the intramural coronary vessels depends in part upon the degree to which they were emptied during the preceding systole Thus the massaging action of myocardial contraction may facilitate coronary flow in much the same way that skeletal muscle contraction has a pumping effect (see Fig 4 Chapter 3)

According to Gregg[20] stimulation of the sympathetic nerve supply to the heart produces a number of effects including (*a*) a marked decrease in systolic flow through the coronary vessels presumably caused by the increased vigor of the ventricular contraction (*b*) a large increase in diastolic coronary flow with a sizable net increase in mean flow (*c*) an increase in the extraction of oxygen from the coronary blood (*d*) increased left ventricular metabolism (*e*) increased cardiac output and total heart work (*f*) marked reduction in systolic and diastolic size of the heart and (*g*) reduced mid diastolic left ventricular pressure The increased coronary flow occurs with little or no elevation of central coronary pressure either with or without changes in heart rate When the work required of the heart is increased by artificial aortic constriction elevated systemic arterial pressure produces an increase in coronary flow, but the accelerated coronary flow begins just *before* any significant change in central coronary pressure occurs Gregg stated[20] However this determination alone is entirely unrevealing as to how the heart is able to obtain an extra influx of blood just before its work increases and how it reduces coronary inflow just before cardiac work is curtailed Here again we are confronted with anticipatory adaptation which will probably remain obscure until more is known of how neural reflex phenomena integrate the various components of the cardiovascular system

Control of Coronary Flow

As in other tissues of the body, blood flow through the coronary artery is increased primarily by reducing resistance to flow through the small vessels Myocardial hypoxia is a powerful stimulus to vasodilatation Under extreme conditions (inhalation of pure nitrogen) the flow may be increased fivefold by this mechanism Increased carbon dioxide or diminished pH have much less effect It is currently believed that the caliber of the coronary vessels depends upon a state of constrictor tone produced by a continuous vagal discharge In chronic experimental preparations, elimination of sympathetic control of the heart produced no demonstrable change in coronary flow but bilateral vagotomy was followed by a markedly accelerated coronary flow, which was not significantly altered by exercise[21] Coronary vasoconstriction is released by reducing vagal discharge and to a lesser extent, by increasing either sympathetic stimulation or circulating epinephrine

CARDIAC ENLARGEMENT

As a result of malfunction or disease the heart may labor under various types of

chronic stress (*a*) an increased volume load due to a sustained increase in ventricular output or valvular insufficiency, (*b*) an increased *pressure load due to arterial hypertension or* semilunar valvular stenosis, (*c*) interference with the delivery of metabolic fuels and oxygen by way of the coronary vessels, and (*d*) destruction or impairment of myocardial elements by coronary insufficiency or toxic effects of bacterial infection (e g, diphtheria) These examples of stress represent reduced efficiency of the cardiovascular system as a whole, characterized by an increased waste of the energy produced by ventricular contraction The cardiac response depends to a certain extent upon the nature of the abnormal load

Ventricular Dilatation

Dilatation of the ventricular chambers is the predominant response to a chronic volume load, a volume load is any condition which imposes a requirement for a sustained increase in stroke volume Right and left ventricular volume loads result from many conditions such as anemia, hyperthyroidism, patent ductus arteriosus, etc or the increased ejection required to compensate for valvular insufficiency with regurgitation Since the left ventricle is designed architecturally as a pressure pump, it is overworked by volume loads The energy release *which is stored or wasted as myocardial* viscosity and interfascicular tension is much greater in the left ventricle than in the right (Chapter 7) Through ventricular dilatation, an increased stroke volume is attained without a corresponding increase in myocardial shortening The greater energy release gained through increased fiber length (Starling's law of the heart) is another advantage gained through dilatation

ACUTE VENTRICULAR DILATATION Acute dilatation of the heart may occur during acute myocarditis due to rheumatic fever non-specific febrile illnesses or toxic disease states Under these conditions, ventricular distention accompanied by signs of heart failure may rapidly develop in patients with previously normal hearts Acute dilatation of the chamber requires an increase in effective filling pressure and in elevated venous pressure, and frequently leads to venous congestion This sequence suggests a rapid diminution of myocardial contractility and *excessive ventricular distention beyond the* normal range

CHRONIC LEFT VENTRICULAR DILATATION There must be an important difference between acute distention and chronic dilatation If progressive dilatation occurs over a long period of time, the ventricular volume may become very large without a significant rise in filling pressure The effective filling pressure of a dilated left ventricle may remain normal for years so long as the heart remains competent Chronic ventricular dilatation is probably not simple stretching *of the wall, the myocardial fibers probably* grow longer so that the blood vessels, connective tissue stroma, and pericardial sac *must also expand by elaboration of new* tissue structure The other components of cardiac reserve are not generally utilized in the cardiac accommodation to a chronic volume load so long as the compensation by dilatation is adequate The presence of ventricular dilatation indicates that the systolic reserve capacity is increased, but not being used The heart rate and the arteriovenous oxygen difference are within normal *limits at rest although they may exceed the* normal both during and following exertion In one sense, ventricular dilatation implies that contractility is either diminished or inadequate

Chronic left ventricular dilatation is almost invariably associated with some degree of myocardial hypertrophy Not only is the weight of the ventricular walls increased by an increased mass of tissue but the myocardial *fibers generally have increased diameter* Ventricular dilatation increases the radius of the circles described by the constituent myocardial fibers so their tension must be correspondingly increased to develop the same intraventricular pressure according to the law of Laplace ($P = T/R$) Thus, pure

dilatation of a chamber without some degree of myocardial hypertrophy rarely occurs If the volume load on the left ventricle can be relieved (by ligation of a patent ductus or excision of an arteriovenous aneurism) the dilated chamber reverts toward normal dimensions often to an amazing degree This change indicates that the adaptive mechanisms of the ventricle are reversible

According to Grant[2] dilatation of the left ventricular wall is not accompanied by a similar dilatation of the mitral valve ring However the papillary muscles chordae tendineae and mitral valve leaflets become longer In spite of very different morphologic characteristics these structures participate almost equally in adapting to the new dimensions of the chamber If such a change *in length did* not occur the traction on the valves by a massively dilated chamber would probably prevent complete closure of the mitral valves during systole Although mitral regurgitation may result *from this* mechanism in acute left ventricular dilatation gradual dilatation apparently *does not* produce valvular insufficiency

Right Ventricular Dilatation The normal right ventricle is particularly suited for the pumping of large volumes of blood against low outflow resistance with minimal myocardial shortening Because of the large surface area per unit volume in the normal right ventricle a relatively small degree of dilatation can accommodate *greatly* increased diastolic and stroke volumes Under these circumstances a *chronic volume load* can be well sustained without dilatation For example a defect in the interatrial septum allows recirculation of blood through the lungs so that the right ventricle may pump two or three times as much blood as the left Patients with such a defect may have a good exercise tolerance without significant right ventricular dilatation so long as the pulmonary resistance *remains* low However a sustained increase in pulmonary blood flow often leads to an increased resistance to the flow of blood through the lungs and pulmonary hypertension The right ventricle adjusts to this pressure load by hypertrophy by thickening of the wall and rounding of the chamber in short by assuming some of the characteristics of the normal left ventricle

Ventricular Hypertrophy

Myocardial hypertrophy is the typical response to chronic pressure load as exemplified by arterial hypertension or semilunar valvular stenosis Under these conditions the intraventricular pressure must be elevated to abnormally high levels during each cycle to eject the normal increment of blood into the arterial trunk Dilatation of the ventricular chamber would *require* an *even* greater myocardial tension in accordance with the law of Laplace ($P = T/R$) Greater contractile force can be attained by the elaboration of additional contractile units Although the myocardial fibers do not multiply in number, their diameter increases as they become packed with more contractile *elements* In patients with a *chronic pressure load* (*essential hypertension*) no direct relationship has been established between the duration and degree of hypertension and the size of the heart[23] Many patients may endure severe hypertension for years and progress to serious heart failure without demonstrable cardiac enlargement Under these conditions the principal compensation to the increased pressure load is myocardial hypertrophy The power of the ventricular contraction is enhanced by the greater number of contractile units and the volume of the chamber remains *relatively* small avoiding *the increased* myocardial tension required by an expansion to larger *systolic* and diastolic volumes

Thus the usual response to a chronic pressure load is myocardial hypertrophy with various degrees of ventricular dilatation unless heart failure should supervene The thickened ventricular walls probably have diminished distensibility requiring a greater effective filling pressure to attain a particular diastolic volume In *other* words the

chronic stress (*a*) an increased volume load due to a sustained increase in ventricular output or valvular insufficiency, (*b*) an increased pressure load due to arterial hypertension or semilunar valvular stenosis, (*c*) interference with the delivery of metabolic fuels and oxygen by way of the coronary vessels, and (*d*) destruction or impairment of myocardial elements by coronary insufficiency or toxic effects of bacterial infection (e g , diphtheria) These examples of stress represent reduced efficiency of the cardiovascular system as a whole, characterized by an increased waste of the energy produced by ventricular contraction The cardiac response depends to a certain extent upon the nature of the abnormal load

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ventricle is hypertrophied than when it is in the normal state However, *the heart rates* in such patients are either normal or elevated so the hypertrophic myocardium is probably suffering some degree of oxygen deficiency This type of analysis indicates that the diameter of myocardial fibers rarely exceeds a value of 32μ because the central core of larger myocardial fibers would not receive adequate oxygen.

Jones-6 measured the weights of the right and left ventricular walls and interventricular septum in a large number of patients with systemic arterial hypertension He concluded that (*a*) only the left ventricle hypertrophies in hypertensive individuals without congestive failure (*b*) with the advent of congestive failure, the right ventricle hypertrophies progressively with the duration of failure both auricles hypertrophy and the left ventricle also continues to increase in weight (*c*) after failure has existed for over three years the two chambers diminish in weight the reduction in weight may be more marked in the left ventricle It is possible that the cases with cardiac failure represent a group separated from the other on the basis of a more marked hypertrophy which has outstripped the capillary bed ' At every turn we encounter examples which indicate that the rate of oxygen delivery to the myocardium limits the cardiac output while the maximum cardiac output limits the amount of physical exertion which can be sustained

In summary it seems appropriate to review components of the cardiac reserve emphasizing the characteristic signs associated with the utilization of various com ponents as they occur in patients with heart disease

SUMMARY

In the normal individual the cardiovascular reserve mechanism provides prompt and effective response to widely varying de mands for blood flow to provide oxygen and metabolic fuels to dissipate heat, for digestion of food for proper function of glands and excretory organs and for other essential functions The maximum oxygen delivery to tissues depends upon four principal *components* of cardiovascular reserve the venous oxygen reserve, the maximum cardiac output which can be sustained, the efficiency of myocardial energy release and the oxygen delivery to the myocardium Depletion of any one of these components diminishes the total reserve deleteriously affecting all other reserve factors The various types of cardiac disease affect total cardiovascular reserve in different ways but the end result is always some reduction in the total oxygen delivery to tissues which can be sustained during physical exertion Thus, diminished exercise tolerance is a common denominator of cardiac disease

The Maximum Oxygen Transport

The total oxygen delivery to the tissues of the body is determined by the average quantity of oxygen extracted from each increment of blood (mean A V oxygen difference) and the systemic blood flow (cardiac output) Thus the total oxygen delivery can be represented by an area determined by the product of the cardiac output and the average oxygen extraction from the blood (Fig 7) The total oxygen delivery at rest amounts to about 250 cc per minute (5 l of blood per minute × 50 cc of oxygen per liter) Tissues may be supplied with increased oxygen by greater cardiac output or by greater oxygen extraction from the blood Since a number of vital tissues must be supplied with blood even though their oxygen extraction is relatively slight (kidneys central nervous system etc) the mixed venous oxygen content rarely falls below some critical value Thus there is a minimal residual oxygen content of blood which is rarely encroached upon except in certain persons with severe cyanosis from congenital malformations of the heart (see Chapter 19) In such instances the tissues apparently accommodate to an existence in an environment of very low oxygen tensions

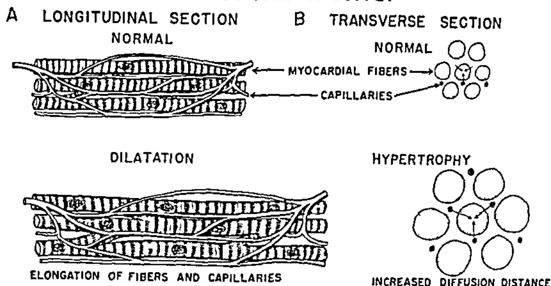


FIGURE 6 *A*, Chronic ventricular dilatation involves elongation of both the myocardial fibers and the coronary capillaries The mass of myocardial contractile units being supplied is greater and the distance traversed by the blood is increased A greater proportion of oxygen in the blood is probably extracted under these conditions

B Ventricular hypertrophy is accomplished by proliferation of contractile units within the individual myocardial fibers The distance of diffusion from the capillaries to the center of adjacent fibers is increased retarding the exchange of various substances particularly oxygen The diameter of myocardial fibers rarely exceeds 32μ even in extreme degrees of hypertrophy

myocardial hypertrophy tends to permit utilization of the systolic reserve capacity with some sacrifice of distensibility On the other hand, ventricular dilatation involves an encroachment on the diastolic reserve capacity with apparently some sacrifice of the contractility, since these distended ventricles fail to empty as completely during systole as the normal Ventricular dilatation probably places some restriction on oxygen delivery to the myocardium, owing to lengthening of the coronary capillaries (Fig 6) Myocardial hypertrophy impairs oxygen delivery to an even greater extent by increasing the diffusion distance from the capillaries to the center of the enlarged myocardial fibers

Oxygen Delivery to Hypertrophied Myocardial Fibers Normal myocardial fibers range from 13 to 16μ in diameter Hypertrophied myocardial fibers may reach 25 to 32μ in diameter, but rarely exceed that value The apparent limitation on hypertrophy of myocardial fibers has been attributed to retardation of oxygen delivery because of the greater diffusion distance to the center of the fibers The relation between the rate of oxygenation and the diameter of nerve fibers was discussed by Hill[24] If a cylinder composed of material similar to a frog's nerve, 7μ in diameter, were suddenly placed in oxygen, 90 per cent oxygen saturation would be attained in about 0 0054 seconds Similar cylinders 0 7 mm in diameter would require 54 seconds for 90 per cent saturation, and those 1 cm thick would attain the same level of saturation after 3 hours The rate of diffusion through tissues varies as the square of the distance, which accounts for the prolongation of the time required for saturation of fibers with larger diameters Harrison[25] reasoned that slower diffusion of oxygen to the center of hypertrophied myocardial fiber would prolong the recovery time required for the fiber to fully regain its energy rich state On this basis, the heart rate should be much slower when the

tion from coronary blood is so great that little oxygen remains after the blood passes through the capillaries. For this reason the principal *mechanism* for increasing oxygen delivery to the heart is increased coronary flow.

Some Conditions Which Limit Maximal Oxygen Transport

A few specific clinical conditions have been selected to illustrate the relations between *these various components of cardiovascular* reserve. The primary effects are schematically illustrated *in* Figure 8 by altering the configuration of the graphs in Figure 7.

ANEMIA. If the hemoglobin concentration of the blood is diminished, the oxygen content of blood may be reduced from 20 volumes per cent to 12 *volumes per cent*. In the systemic capillaries a smaller amount of oxygen is extracted from each 100 cc increment of blood since the mixed venous oxygen content is not decreased below some critical value. Thus the principal adjustment

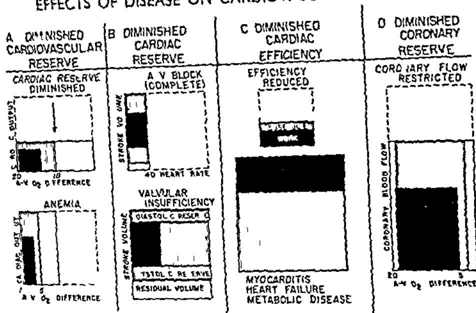


FIGURE 8 The effects of various cardiac abnormalities on the cardiovascular reserve are schematically illustrated by appropriate modifications of Figure 7.

A Diminished cardiac reserve *limits the maximal* amount of oxygen which *can* be delivered to the tissues. More complete utilization of venous oxygen *reserve* and restricted tolerance to exertion *are obvious* sequelae to this condition. Most forms of heart disease diminish *cardiac* reserve in one way or another. The cardiovascular reserve is also depleted by conditions which *interfere with* the transport of oxygen by the blood such as occur in anemia. Some of the cardiac reserve *capacity is* used at rest and a smaller increment is therefore available during increased activity.

B Cardiac reserve *can* be *diminished* in many ways. However, complete A-V block with the heart rate fixed at 40 beats per minute is a rather pure form of restriction of the heart rate response. Under these conditions, cardiac output can be increased only through augmented stroke volume. Valvular insufficiency is a common source of diminished stroke volume reserve. The affected ventricle *must* pump a quantity of blood equal to flow through the vessels plus the amount which regurgitates through the valve. The stroke volume is greatly increased and the reserve is depleted. Constrictive pericarditis *tends to limit* stroke volume in a very direct way.

C The conditions which deleteriously affect mechanical efficiency of the heart have not been completely tabulated. It seems clear that *myocarditis*, heart failure and certain metabolic diseases may diminish all the other components of cardiovascular reserve by reducing cardiac efficiency. This places an added load on the coronary oxygen delivery as *well as* restricting the maximal stroke volume and oxygen transport.

D Restricted coronary flow limits oxygen delivery to the myocardium. In this way *it* diminishes total *energy* release by the ventricles and reduces reserve cardiac output and the maximal sustained *oxygen* transport by the blood.

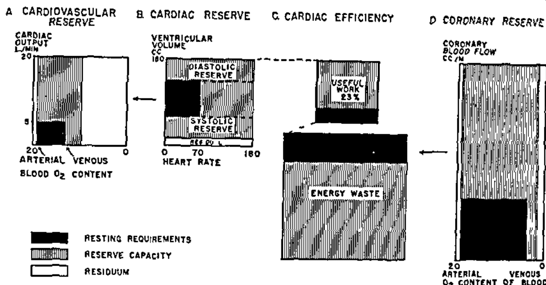


FIGURE 7 *A* The cardiovascular reserve indicated by the rectangular area covered by vertical lines is the product of cardiac output and the arteriovenous oxygen difference This area represents the total oxygen delivery to the body The resting A V oxygen difference is normally about 5 volumes per cent and rarely exceeds 9 to 10 volumes per cent The cardiac output can be increased from four to sevenfold depending on physical condition

B The cardiac output reserve is the maximal sustained cardiac output determined by the product of stroke volume and heart rate (see Fig 2)

C Cardiac efficiency varies considerably among normal individuals but if it remains constant at different work loads every increase in cardiac output is attended by an even greater quantity of energy wasted Under some conditions the efficiency is improved when cardiac output is increased

D The total amount of energy released by the heart (C) is limited by the total oxygen delivery to the myocardium—the product of coronary flow times A V oxygen difference Since oxygen extraction is extensive in the coronary capillaries of normal resting individuals little venous reserve is available and increased coronary flow must accommodate for increased total energy expenditure including greater energy waste

Cardiac Output

The cardiac output is determined by the product of the stroke volume and the heart rate At rest, a heart rate of slightly more than 70 beats per minute and a stroke volume of about 70 cc of blood accounts for a cardiac output of about 5 l per minute The stroke volume may be increased by greater diastolic distention or by more complete systolic ejection (Figs 2, 7*B*)

Efficiency of the Heart as a Pump

The cardiac output represents only about 20 per cent of the total energy release, the remainder of the energy being wasted in the form of friction, energy lost in chemical reactions, etc (Figs 3, 7) When cardiac output increases, the energy waste is also greater and may reach very large values during maximal effort

Myocardial contraction represents the conversion of chemical energy into mechanical energy During each cardiac cycle the contractile mechanisms must be restored to the high-energy, resting state Obviously the total energy *restoration must* equal the total energy release over a period of time Under these circumstances the rate at which oxygen reaches the contractile units is a limiting factor in the process of attaining the high energy state

The Total Oxygen Delivery to the Myocardium

The oxygen delivery to the myocardium depends upon the same factors which determine oxygen delivery to the other tissues of the body, namely, the blood flow and the average quantity of oxygen removed from each increment of blood The oxygen extrac-

flow and oxygen delivery to the myocardium Since cardiac efficiency is considerably reduced when a particular level of cardiac output is attained predominately by tachycardia the energy waste is greater and the total energy expenditure must be increased

REDUCED CARDIAC EFFICIENCY Although the normal heart may operate with 20 per cent efficiency certain disease processes reduce the efficiency of cardiac contraction by means *other* than the effects of tachycardia mentioned above This means that energy wastage and total energy expenditure must be greater, that the energy restoration and oxygen delivery in the myocardium must be accelerated and that the cardiac reserve is curtailed (Fig 8C) For example some young patients with apparently normal hearts may develop myocarditis and in a short space of time develop the classic signs and symptoms of heart failure including severe cardiac enlargement venous congestion and edema Patients with *serious* degrees of heart disease may compensate for long periods of time before signs of heart failure appear One alteration which may precipitate an attack of heart failure is a reduction in the efficiency of cardiac contraction as has been indicated in direct measurements of myocardial oxygen utilization in relation to the work of the heart

DIMINISHED CORONARY OXYGEN DELIVERY Obstruction or occlusion of the coronary arteries impedes blood flow to the myocardium and restricts the quantity of oxygen which can reach the contractile units (Fig 8*D*) In addition to direct mechanical interference with coronary flow, oxygen delivery may be retarded by a number of other circumstances such as hypertrophy of the myocardial fibers diminished pressure gradient along the coronary arteries (aortic stenosis and aortic insufficiency) myocarditis with interstitial edema and tachycardia Indeed inadequate myocardial oxygenation may be the prime limitation on the cardiac output in many pathologic conditions of the heart and circulation

In view of the fact that most forms of heart disease affect more than one component of the cardiovascular reserve it is not surprising that similar signs and symptoms develop during heart failure, regardless of the nature and cause of the cardiac disease

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to a reduced A-V oxygen difference caused by anemia is an increase in the cardiac output (Fig 8A) Since the cardiac output is increased at rest, the reserve is diminished and the maximal sustained increase in cardiac output is less than normal The increased systemic flow is not as effective as normal oxygen extraction in supplying the tissue because of the reduced oxygen capacity of the blood The arterial blood entering the coronary capillaries also carries a reduced quantity of oxygen, impairing the oxygenation of the myocardium Further, cardiac acceleration is more pronounced with moderate exercise than normal Thus, significant anemia deleteriously affects a number of components of cardiovascular reserve oxygen transport, total energy release, and total oxygen delivery to the myocardium

COMPLETE A-V BLOCK When the atrioventricular node blocks all impulses of atrial origin, a site in the ventricle usually assumes the role of pacemaker It emits impulses at a slow but fairly constant rate of about 40 to 50 per minute even during exertion Thus, the cardiac reserve is limited because the normal cardio-acceleration does not occur in response to increased requirements for greater peripheral blood flow (Fig 8B) As the heart rate is slower than normal, the stroke volume is excessive even with normal resting cardiac output Thus, the stroke volume reserve is diminished and compensatory acceleration is abolished With such extreme limitation in cardiac reserve, compensation to exertion must produce an abnormally increased A-V oxygen difference in the peripheral blood If the A-V block persists, the ventricles often dilate because of the constant requirement for increased stroke volume Dilatation produces elongation of the coronary capillaries and may produce more oxygen extraction of coronary blood Unfortunately, A-V block is commonly caused by coronary insufficiency or occlusion Impeded oxygen delivery to the myocardium may well limit the energy restoration and here, again, several components of cardiac reserve may be affected

VALVULAR INSUFFICIENCY Regurgitation of blood through incompetent valves in the heart always imposes an abnormal volume load on the involved ventricle The blood which surges back into the atrium through incompetent atrioventricular valves during ventricular systole cannot contribute to the oxygenation of tissues Similarly, blood flowing back into a relaxed ventricle through faulty semilunar valves is not effective in oxygen transport To fully compensate for regurgitation of blood through incompetent valves, the stroke volume of the affected ventricle must increase to equal the sum of regurgitant volume plus the normal flow requirements of the body as a whole If the resting stroke volume is significantly increased, the stroke volume reserve is correspondingly diminished during exertion (Fig 8B) Furthermore, the total quantity of regurgitant flow per minute is probably increased during greater cardiac output Thus stroke volume reserve tends to be depleted by valvular insufficiency The principal compensation for valvular insufficiency is ventricular dilatation by which augmented stroke volume can be attained by relatively slight increase in the degree of myocardial shortening In contrast, constrictive pericarditis limits stroke volume reserve by directly interfering with increased diastolic filling

ADHESIVE PERICARDITIS Diastolic distention of the ventricles may be seriously restricted by the thickened, adherent pericardium produced by chronic pericarditis Under these conditions, diastolic reserve volume is extremely limited and the principal mechanism for increasing stroke volume is greater contractility The effective filling pressure is markedly elevated in most instances even though this is of little avail Marked venous congestion is a characteristic sign of the condition Furthermore, the stroke volume reserve is so depleted that the principal adjustment in cardiac output is cardio-acceleration Thus, the heart rate is very labile, reflecting every change in output Tachycardia interferes with coronary

The Etiology of Congestive Failure

Patients with heart disease may have neither symptoms nor external signs during routine activity so long as they remain compensated This term actually means that the cardiovascular reserve capacity is sufficient for the range of activity usually encountered by a particular patient The diminished cardiac reserves become manifest during more intense exertion by the appearance of breathlessness perceptibly forceful heart beat and fatigue at levels of exercise which could previously be tolerated with ease As the cardiovascular reserves become further depleted the maximal sustained cardiac output is seriously curtailed and a greater proportion of oxygen transport is attained by oxygen extraction which widens the arteriovenous oxygen difference The final stages are reached when the cardiac output is barely adequate for the metabolic requirements at rest As various components of the cardiac reserve are progressively depleted diminished exercise tolerance is the most obvious symptom In many patients with advanced heart disease the heart remains compensated for a long time and the signs and symptoms of congestive heart failure appear abruptly without any obvious precipitating cause Some patients with moderately advanced heart disease may display severe signs of congestive heart failure while other individuals with apparently more serious cardiac impairment remain compensated

The factors involved in the transition from compensation to decompensation have not been clearly elucidated The failing ventricle has been described[1] as having a slower pressure rise during isometric contraction a lower systolic peak pressure a larger diastolic size a higher filling pressure and diminished efficiency This description is consistent with a reduction in "contractility" as defined previously (Chapters 6, 7) The reduction in the mechanical efficiency of myocardial contraction (see Chapter 8) is an important factor in heart failure A failing heart does not fully use the energy derived from the breakdown of glucose Detailed investigation of the changes in myocardial metabolism should clarify the nature and significance of ventricular failure

Left ventricular failure most commonly occurs in adults with acquired heart disease of various types Left ventricular decompensation produces pulmonary hypertension which imposes a pressure load on the right ventricle and frequently leads to right ventricular failure Primary right ventricular failure usually occurs in children with certain congenital malformations of the heart

LEFT VENTRICULAR FAILURE

Depletion of the left ventricular reserve capacity should curtail the maximum sustained cardiac output in accordance with the principles discussed in Chapter 8 This fact has been clearly established by several studies utilizing cardiac catheterization to measure cardiac output in normal individuals and in patients with heart disease

Hickam Cargill and Golden[2] studied the cardiovascular responses of patients with heart disease and normal subjects and arrived at the following conclusions (1) In normal persons during exercise there is an increase in both cardiac output and arteriovenous oxygen difference but the increase in cardiac output predominates (2) in persons with congestive heart failure there is little or no increase in the cardiac output during

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24 Hill A V The diffusion of oxygen and lactic acid through tissues Proc Roy Soc. Lond, B104 39–96 19 8
25 Harrison T R Failure of the Circulation Baltimore Williams & Wilkins Co 1939
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sure and an augmented pulmonary congestion with a paradoxical reduction in stroke work. On this basis pulmonary congestion should be exaggerated by exercise. However the applicability of such curves to human patients remains to be directly demonstrated. In the meantime the association of heart failure with increased ventricular filling pressure must be recognized, but cannot be adequately explained.

The reservoir capacity of the pulmonary vascular tree is generally believed to be smaller than that of the systemic venous system. Cournand[5] estimated that the lungs normally contain only about 5 per cent of the total blood volume while the systemic veins contain about 55 per cent. Accordingly he concluded that pulmonary congestion could be caused by a transfer of blood from the systemic venous system into

PULMONARY CONGESTION FROM LEFT VENTRICULAR FAILURE

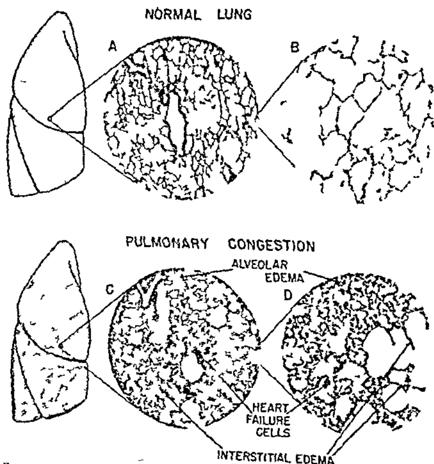


FIGURE 1 *A* The normal lung is partitioned by delicate alveolar membranes into microscopic air sacs. This structural organization provides a tremendous surface area for gas exchange.
B The alveolar membranes are exceedingly thin and blood in capillaries coursing through them comes into almost direct contact with the alveolar air.
C Pulmonary congestion and edema seriously impede aeration of the alveolar sacs and gas exchange between alveolar air and blood. The presence of edema fluid in alveolar sacs renders them almost functionless and the foaming effect of the fluid impedes respiratory gas movement.
D Accumulation of fluid within the alveolar walls (interstitial edema) produces an increase in the distance of diffusion, so that gas exchange between alveolar air and blood is slowed even in alveoli which contain no fluid. (Microscopic slides were obtained through courtesy of Dr Theodore Thorson, Department of Pathology, University of Washington.)

exercise, but there is a large increase in arteriovenous oxygen difference (3) in frank chronic congestive heart failure the resting output is the greatest that can be consistently maintained, but even at rest this output may not be great enough to supply the tissues with blood at a rate normally commensurate with their metabolic needs" Briggs, et al[3] measured many variables including cardiac output, blood volume, thiocyanate space, and filling pressures of the heart They found that the oxygen saturation of mixed venous blood correlates best with the clinical status in compensated and uncompensated patients

The ventricles adjust to volume loads chiefly by dilatation and to pressure loads chiefly by myocardial hypertrophy However, adjustments to either type of load usually involve varying combinations of both mechanisms Both ventricular dilatation and hypertrophy presumably reduce the distensibility of the chamber and lead to increased diastolic pressures Elevated left ventricular diastolic pressures promote pulmonary hypertension and congestion

Pulmonary Congestion from Left Ventricular Failure

Normal lungs are delicate, spongy, crepitant and resilient Their color is uniformly salmon pink in young individuals, but with advancing age, accumulation of carbonaceous substances produces a tinge of slate gray Microscopic sections of inflated pulmonary parenchyma show the delicate alveolar membranes partitioning the alveolar ducts and air sacs (Fig 1*A*) The blood in the alveolar capillaries comes into very close proximity with the alveolar air, so the distance of diffusion for gaseous exchange is extremely short (Fig 1*B*)

The lungs of patients who have died after chronic left ventricular failure are engorged with blood, heavy, discolored tough and indurated The normal resilience is diminished because connective tissue has proliferated within the parenchyma The alveolar membranes are thickened and edematous, increasing the distance between the alveolar air and capillary blood (Fig 1*C*) Many alveoli are partially or completely filled with edema fluid, which would seriously impair respiratory exchange Scattered throughout the alveolar spaces are phagocytes containing a yellow brown pigment (hemosiderin) derived from erythrocytes extravasated into the alveolar spaces The caliber of the small bronchial airways may be diminished by congestion and edema of the mucosa, and by increased excretion of mucus Thus, gas exchange in the lungs of patients with chronic left ventricular failure is impeded in three ways (*a*) by increased resistance to the flow of air in and out of the alveoli, (*b*) by alveolar flooding with edema fluid, and (*c*) by retarded diffusion of gases from alveolar air to capillary blood by interstitial edema (Fig 1*D*)

Etiology of Pulmonary Congestion Accumulation of blood within the pulmonary vessels is associated with increased pressure in these channels Since the lungs function as a blood reservoir (see Chapter 4) the pulmonary vasculature, particularly capillaries and veins, is highly distensible The pressure in the capillaries and veins must exceed the diastolic pressure in the left ventricle, which is the point of outflow from the pulmonary vessels The pressure gradient from pulmonary artery to left ventricle is so shallow (6 mm Hg) that any increase in left ventricular filling pressure produces a generalized increase in pulmonary vascular pressures (Fig 2) An elevated ventricular filling pressure has been generally attributed to the descending limb on Otto Frank's pressure volume curve (Fig 2, Chapter 6) This curve suggests that beyond some critical diastolic volume, further increase in filling pressure is accompanied by progressive reduction in contractile tension When Sarnoff and his associates[4] restricted coronary flow, they observed such a descending limb in their 'modified Starling curves' (Fig 2, Chapter 6) If the failing heart behaves this way, physical exertion produces an increased diastolic filling pres-

improved the condition once established Ganglionic blockade on the contrary, produced slight lowering of arterial blood pressure and the pulmonary vascular pressures *returned to normal* Judging from the functional characteristics of the systemic venous and arterial systems (Chapter 2) this observation suggests that sympathetic discharges produced by the fibrin induce peripheral vasoconstriction and increased venomotor activity which altered the capacity and distensibility of the systemic venous system and shifted large quantities of blood into the pulmonary capillaries and veins (see Fig 3)

Symptoms from Pulmonary Congestion

The most common presenting symptom of left ventricular insufficiency is dyspnea on exertion This shortness of breath is characterized by rapid shallow respiration in contrast to the deep full inspiration which is the normal respiratory response to exercise After varying periods of time the amount of exercise required to induce dyspnea progressively decreases Eventually the individual may develop respiratory distress when he lies down (*orthopnea*) Then the patient can breathe comfortably only with his head and trunk erect, even during sleep For unknown reasons *orthopnea* is the initial symptom in many patients with left ventricular insufficiency, particularly that caused by *hypertension or coronary* insufficiency Such patients are apt to develop attacks of respiratory distress similar to asthma with forced inspiratory and expiratory movements (cardiac asthma) and associated with coughing or choking and expectoration of blood tinged sputum Thus the fundamental symptoms of left ventricular failure are those of respiratory dysfunction associated with pulmonary congestion

Effects of Pulmonary Congestion on Gas Exchange. Blood in the pulmonary capillaries can become oxygenated only if oxygen can diffuse rapidly from the alveolar spaces through the intervening membranes to reach the blood Rapid diffusion of dissolved gases occurs over very short distances in response to steep con

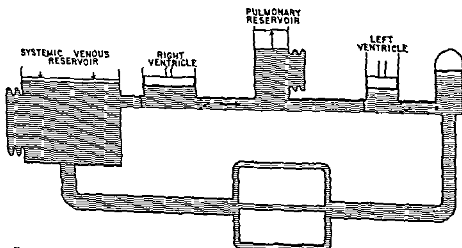


Figure 3 According to *current theory* the capacity of the systemic venous reservoir is much larger than that of the pulmonary *venous reservoir* Under these conditions transfer of small quantities of blood from the systemic circulation would produce a relatively large *increase* in pulmonary vascular volume and pressure Very slight imbalance between the output of the *right ventricular chamber* (*volume* pump) and the left ventricle (pressure pump) could theoretically produce significant pulmonary congestion A sustained increase in left ventricular filling pressure could theoretically produce *chronic* pulmonary congestion without appreciable increase in total blood volume

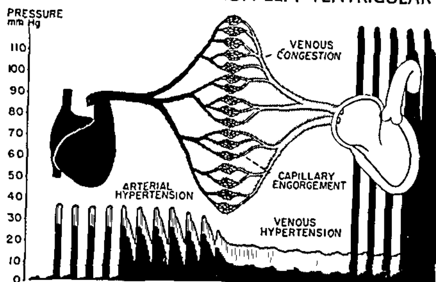


FIGURE 2 The pressure gradient from pulmonary arteries to left atrium is very slight (about 6 mm Hg) so any increase in left ventricular filling pressure is immediately reflected throughout the pulmonary vascular tree Increased pressure in distensible pulmonary veins and capillaries produces marked distention and engorgement Thus pulmonary venous and capillary hypertension produces pulmonary congestion and pulmonary edema if the pressures reach sufficient height

the pulmonary vascular tree (Fig 3) If the right ventricular output exceeds left ventricular output, a large quantity of blood would be quickly transferred to the lungs *from the systemic venous reservoirs* The right ventricle is so well adapted as a volume pump that transient imbalance between right and left ventricular output could produce some degree of pulmonary congestion under many circumstances, e g, during the transition from rest to physical exertion (see Chapter 6) More recent evidence indicates that both the capacity of the pulmonary vascular tree and the quantity of blood shifted between the lungs and the systemic *circulation (reservoir function) are much* greater and more important than is generally recognized (see Chapters 3 and 4) Accumulation of blood within the pulmonary vascular tree is probably more extensive in patients having increased total blood volume (i e, right ventricular failure)

Although the clinical picture of pulmonary congestion and edema is most commonly encountered in patients developing left ventricular failure, it is sometimes seen *in patients with* head injury [6] Similar effects can be produced by a wide variety of experimental procedures involving the central nervous system, such as increasing the intracranial pressure [7] injecting fibrinogen[8] or veratrine[9] intracisternally, or making discrete *lesions in the preoptic region of the* hypothalamus [10] The mechanisms by which these neural factors become expressed as pulmonary congestion and edema have not been clarified Paine et al [11 12] demonstrated elevated pulmonary vascular pressures in pulmonary edema precipitated by embolism of cerebral vessels similar hemodynamic effects presumably occur when other cerebral factors result in the same functional disturbances

For example, in the experiments of Sarnoff et al, [13 14] intracisternal injection of fibrin produced severe pulmonary edema presumably due to nonspecific *stimulation of* the cardiovascular centers Both arterial and venous pressures increased markedly in both the pulmonary and the systemic circulation The pulmonary venous pressure rose as high as 70 mm which was considered sufficient to explain the production of pulmonary edema without any change in capillary permeability Vagotomy neither prevented these changes nor significantly

extremities The veins are distended because of the high hydrostatic pressures (see Chapter 3) During the day, fluid filters from the capillaries into the tissue spaces in the dependent parts in response to the high intravascular pressures When a person lies down the pressure in these vessels diminishes and the excess fluid is reabsorbed expanding the blood volume at night At the same time the blood which had distended the peripheral veins is redistributed and much of it accumulates in the pulmonary tree In normal individuals, this shift of blood into the lungs produces no disturbance However in patients with antecedent pulmonary congestion due to left ventricular failure the added load induces dyspnea in th reclining position The patients prop themselves up in bed to avoid the unpleasant consequences of reclining The etiology of dyspnea is schematically illustrated in Figure 4

Symptoms from Bronchial Congestion

The pulmonary and bronchial arteries serve independent capillary networks except at the respiratory bronchioles and alveolar ducts However all the alveolar capillaries and most of the bronchial capillaries drain into the pulmonary veins Elevation in left ventricular diastolic pressure and pulmonary venous pressure is accompanied by congestion in those bronchial vessels which drain by this route Engorgement of the mucous membranes produces edema and encroachment on the airways These events tend to impede movement of air in and out of the lungs (Fig 4) Greater muscular effort is required for respiratory ventilation

ETIOLOGY OF RESPIRATORY SYMPTOMS FROM PULMONARY HYPERTENSION

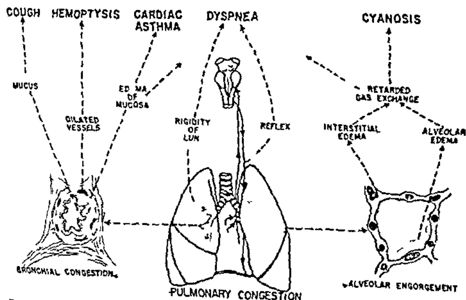


FIGURE 4 Since most bronchial capillaries drain by way of the pulmonary veins congestion develops simultaneously in alveolar and bronchial vascular networks Bronchial congestion tends to stimulate production of mucus leading to a productive cough The distended bronchial capillaries may rupture so the patient coughs up blood-tinged sputum (hemoptysis) Edema of the bronchial mucosa increases resistance to air flow producing respiratory distress similar to asthma Dyspnea results primarily from reflexes initiated by vascular distention, but may be supplemented by increased rigidity of the lungs and by impaired gas exchange resulting from interstitial edema and accumulation of fluid in alveolar sacs (see Fig 1) Cyanosis is not consistently observed even in patients with severe pulmonary edema (see text)

centration gradients An increased distance of diffusion across the alveolar walls theoretically retards the rate of oxygen transfer For this reason, relatively thin layers of extravascular fluid interposed between the capillaries and the alveolar air should seriously reduce the efficiency with which the blood is oxygenated (Fig 1C) Pulmonary edema results from excessive filtration *of fluid through the pulmonary capillaries* in accordance with Starling's hypothesis of capillary fluid balance (see Chapter 2 and *Etiology of Peripheral Edema*, this chapter) Flooding of alveolar spaces interferes with aeration of both the alveolar air cells and the blood

Interference with gas exchange between the alveolar air and the pulmonary capillary *blood may well contribute to cyanosis* appearing in the terminal stages of left ventricular failure Since cyanosis is neither a common nor a prominent feature of pulmonary congestion, the extreme degrees of pulmonary edema found at postmortem examination (Fig 1C) may not necessarily be characteristic of most cardiac patients during life

The presence of fluid in the airways of the lungs is detected clinically by auscultation of the chest The presence and distribution of rales is generally considered a reliable indication that pulmonary edema is present However, Vitale et al[15] found a poor correlation between the auscultatory signs of pulmonary edema and the arterial oxygen saturation For example, some patients with minimal signs over the base of the lungs had lowered oxygen tension while seven of twelve patients with acute pulmonary edema and bubbling rales over all lung fields had arterial saturations of above 93 per cent

DYSPNEA In the past, dyspnea was attributed to diminished oxygen and increased carbon dioxide content of the arterial blood reaching the respiratory centers There is no doubt that inhalation of gas mixtures with either low oxygen tension or increased carbon dioxide concentration results in stimulated respiratory activity However, *under these conditions, increased pulmonary* ventilation is accomplished by deep inspiratory excursions rather than by rapid shallow breathing, which typifies dyspnea Further, dyspnea occurs in patients with left ventricular decompensation without any evidence of pulmonary edema and with normal arterial oxygen and carbon dioxide levels Thus, dyspnea cannot be ascribed *solely to interference with the primary func-*tion of the pulmonary circulation, namely, gaseous exchange between the blood and the alveolar air

Harrison et al[16 17] demonstrated that artificially induced pulmonary congestion in dogs produced rapid shallow breathing which disappeared after section of the vagi They postulated that such dyspnea resulted *from reflex stimulation of respiratory activity* initiated by stretch receptors responding to distention of vascular channels within the thorax Mechanical factors may also be invoked to explain the rapid shallow breathing in response to pulmonary congestion For example, Drinker et al[18] described the turgidity of the lungs produced by artificial pulmonary congestion The lungs resembled *erectile tissue in that they became rigid* and inelastic when engorged with blood Further, the lungs of patients with chronic pulmonary congestion often become indurated by the proliferation of supporting connective tissue While the fibrotic reaction may supply additional external support to the pulmonary vessels, it also tends to reduce the mobility and elasticity of the lungs Under these conditions, increased effort is required to inflate and deflate the lungs Asked to breathe in and out as rapidly and deeply as possible for some 15 seconds (maximal breathing capacity), patients with *left ventricular failure manifest a reduced* ability to increase their respiratory minute volume However, Richards[19] demonstrated that ambulatory patients with exertional dyspnea may retain fairly good maximal breathing capacity

ORTHOPNEA When the body is erect blood tends to accumulate in the dependent

congenital anomalies produce recirculation of blood through the lungs so that the right ventricular output consistently remains two or three times that of the left ventricle Such patients may have an essentially normal exercise tolerance and, in them, right heart failure is brought about by pulmonary hypertension which frequently develops in response to excessive pulmonary blood flow (see Chapter 19) Thus, the principal cause of right ventricular failure is a chronic pressure load which may result from a number of conditions including (a) left ventricular failure with pulmonary congestion and hypertension (b) mitral stenosis (c) primary disease of the lung with pulmonary hypertension and (d) pulmonary valvular stenosis

Right Ventricular Response to Chronic Pressure Loads

In response to sustained pressure loads, two significant changes occur in the right ventricular chamber myocardial hypertrophy and a change in the configuration of the right ventricular cavity As the free wall of the right ventricle thickens the chamber becomes more rounded and the right ventricle assumes some of the characteristics of the left ventricle However, the coronary supply to the right ventricle is limited in comparison to that of the left ventricle In the process of accommodating to a chronic pressure load the right ventricle loses flexibility as a volume pump and suffers some deficiency of coronary supply This coronary supply is particularly important under conditions in which the pulmonary arterial pressure approaches or exceeds normal systemic arterial pressure

Pathologic Evidence of Right Ventricular Failure

In contrast to left ventricular incompetence right ventricular failure is manifested in external signs rather than in subjective symptoms Fully developed right ventricular failure can be recognized from evidence of generalized systemic venous congestion and the development of peripheral edema

Venous Congestion Since blood tends to accumulate in those portion of the systemic venous system with the greatest distensibility in relation to the venous pressure the most obvious engorgement occurs in the systemic venous reservoirs the liver spleen splanchnic bed skin and the central and peripheral venous channels

The liver characteristically enlarges in right ventricular failure extending well below the right costal border and may descend below the level of the umbilicus Often the engorged liver is tender on palpation and occasionally *is the site of spontaneous* abdominal pain The periportal sinusoids of the liver are engorged with blood The degree of congestion tends to diminish from the periphery of the lobules toward the hepatic veins (Fig 5) Chronic hepatic congestion may produce proliferation of connective tissue stroma with reduction in the size of the liver The organization of the liver may be seriously disrupted by diffuse necrosis and scarring which produce the pathologic picture of cirrhosis. It is often difficult to distinguish cirrhosis from other causes Chronic congestion of the liver is occasionally associated with evidence of dysfunction in the form of increased bilirubin in the blood or even perceptible jaundice Bromsulphalein may not be as rapidly *extracted from the blood* under these conditions A seriously engorged liver may contain such large quantities of blood that pressure over the organ may significantly distend the superficial cervical veins even when the patient is semi-erect.

The spleen tends to become enlarged during the development of hepatomegaly presumably because they both have reservoir function and a common venous drainage system However an enlarged spleen is not as obvious as an enlarged liver

The kidneys are enlarged firm and dark red The capillaries in the glomeruli and around the tubules tend to be engorged

and the maximum breathing capacity may be impaired This sequence of events may contribute to the shortness of breath by a mechanism which closely resembles the asthma produced by allergic reactions

A productive cough is a prominent symptom in congestive heart failure The increased production of mucus by congested bronchial mucosa is a logical explanation for this complaint Although coughing is not *a particularly effective mechanism for removing* fluid from the alveoli, edema fluid transported to bronchial airways may be eliminated by this mechanism Blood-tinged sputum is frequently noted and was formerly explained on the basis of extravasation of erythrocytes into the alveolar sacs Hemoptysis is now more frequently attributed to small hemorrhages from the congested bronchial mucosa

Symptoms from Restricted Cardiac Output

Although the classic symptoms of left ventricular failure result from pulmonary dysfunction, restricted cardiac output reserve is an essential feature of this condition When the resting cardiac output is diminished, the blood flow through virtually all regions of the body is curtailed to some extent and the oxygen extraction is correspondingly increased (see Fig 1, Chapter 8) Such depletion of the venous oxygen reserve means that the oxygen tension in these tissues must be subnormal One would certainly expect evidences of dysfunction to result from such a state For example restricted blood flow through skeletal muscle should lead to weakness and fatigability Richards[19] directed attention to the fact that patients exercise tolerance may be limited by fatigue or exhaustion as well as by the accompanying dyspnea, from which it must be distinguished Fatigue is difficult to *define or* describe and is very easily prevented by voluntary restriction in activity to avoid the unpleasant sensation For this reason, relief from weakness or fatigability is most readily recognized by patients whose cardiac condition has been rather suddenly improved, e g , by mitral valvulotomy The sensation of fatigue subjectively stems directly from exercising muscle, and is generally ascribed to oxygen debt and local deficiency in blood flow *A simple experiment* demonstrates that this is an oversimplification If a subject rhythmically flexes his finger against a resistance until fatigue prevents his continuing this exercise, electrical stimulation *of the nerve to the exercising muscle* promptly restores contractions as powerful and rapid as those performed at the onset of the exercise In other words, the fatigue which prevented continuing exercise is not localized in the nerve or exercising muscle but in the central nervous system, the origin of the impulses which drove the muscle

Diminished blood flow through the splanchnic bed might also interfere with gastro-intestinal activity Actually, indigestion is a fairly common complaint in older patients with heart disease, but it is neither distinctive nor consistently observed Most older patients with advanced heart disease might well have similar gastro-intestinal complaints without any heart disease

The kidney is one tissue where the blood flow always remains very large in relation to the oxygen extraction It seems significant that the renal arteriovenous oxygen difference rarely exceeds 3 to 4 cc per 100 cc of blood, even in patients with full-blown congestive heart failure (Fig 1, Chapter 8) Although renal dysfunction leads to retention of salt and water and the production of generalized venous congestion and peripheral edema the cause is probably not insufficient oxygenation of the tissue since the kidney must actually work excessively during abnormally great reabsorption of salt and water (see *Etiology of Peripheral Edema*, below)

RIGHT VENTRICULAR FAILURE

The right ventricular chamber is so well adapted as a volume pump that it rarely fails as a result of a pure volume load Certain

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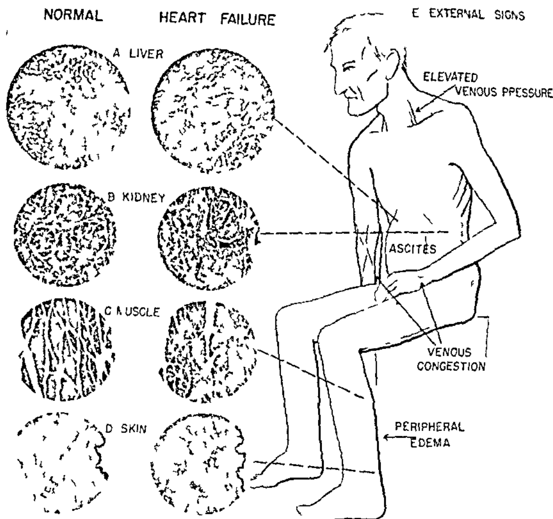


FIGURE 5 Microscopic sections from a patient who died during an attack of congestive heart failure are compared with those from a young adult killed in an automobile accident

A The liver is engorged with blood distending the liver sinusoids in the periportal regions (around the periphery of the photomicrograph)

B The congested kidney is characterized by engorgement of both the glomerular and the peritubular capillaries

C Normally the skeletal muscle fibers are packed so tightly that the cell borders cannot be readily distinguished with low power magnification Edema fluid may force the fibers apart so they stand out individually

D Edematous skin becomes greatly thickened and waterlogged The organization of the connective tissue appears to be disrupted

E External signs of advanced congestive heart failure are obvious on superficial inspection Elevated venous pressure is evidenced by distention of the jugular vein in the erect position and prominence of peripheral veins Ascites produces increased abdominal girth Pitting edema tends to be localized in dependent parts (The slides for this illustration were obtained through the courtesy of Dr Theodore Thorson Department of Pathology and Dr E C Roosen Runge Department of Anatomy University of Washington)

(Fig 5) Histologic demonstration of such engorgement is difficult because congestion in the kidney frequently occurs at the time of death from many causes

The capacious splanchnic bed tends to become engorged in association with hepatomegaly and splenomegaly because blood from the mesenteric veins passes through the liver Such splanchnic engorgement generally produces neither symptoms nor external signs

Distention of the superficial veins is an early sign of venous congestion Since the level of zero effective venous pressure is

normally within the thorax the cervical veins are collapsed when the individual is erect Generalized engorgement of the venous channels is accompanied by elevated central venous pressure so the level of zero effective venous pressure is higher Under these circumstances the jugular vein remains distended even when the patient is erect. The earliest sign of central engorgement may be elicited by gradually elevating the patient from the supine to the sitting position and observing the level of the transition between collapse and distention of the jugular vein above the sternal notch or phlebostatic axis (see Fig 2 Chapter 10) Alternatively the hand can be held dependent until the dorsal veins are distended then elevated gradually so that the level at which the veins become emptied can be observed Abnormal distention of veins may be detected before there is any obvious liver enlargement or peripheral edema These procedures provide a rather crude measure of venous pressure It is preferable to measure venous pressure directly by methods described in Chapter 10 The normal venous pressure in the median basilic vein of normal adult males ranges from 5 to 14 cm of water with the average being 9 7 cm[20] In any particular subject variations in venous pressure occur under many conditions including age muscular activity respiration time of day administration of fluids etc A single determination of venous pressure under standard conditions is often meaningless in assessing the presence or degree of congestive heart failure However serial measurements have value in revealing the course of the development and regression of heart failure Changes in venous pressure occur much more promptly than other pathologic signs and symptoms of congestive heart failure so the correlations among them may be somewhat obscured In other words, elevated venous pressure often occurs well in advance of external signs of venous congestion or peripheral edema During recovery it may return to the normal range before the other manifestations have completely disappeared An authoritative discussion of venous pressure measurement and interpretation has been presented by Burch [6]

CYANOSIS Cyanosis is severe in certain patients and imperceptible in others for no obvious reason Since the skin is a major venous reservoir its blood flow may be curtailed as part of the general conservation of flow particularly if the cardiac output is diminished Slow cutaneous flow produces the so-called 'stagnant' anoxia with more complete oxygen extraction and diminished oxygen content of cutaneous venous blood If the quantity of reduced hemoglobin in cutaneous vessels drops below 5 gm per 100 cc of blood cyanosis becomes perceptible Increased quantity of blood in the skin (congestion) probably emphasizes cyanosis which might otherwise be overlooked Further left ventricular failure with pulmonary congestion and edema may interfere with the oxygenation of arterial blood [15] If the arterial blood entering the capillaries has a diminished oxygen content the quantity of reduced hemoglobin in venous blood is more apt to reach levels above 5 gm per 100 cc of blood

For these reasons cyanosis would be anticipated in patients with advanced cardiac failure involving both right and left ventricles but this prediction is not consistently verified A more detailed discussion of cyanosis is presented in relation to congenital heart disease in Chapter 19

PERIPHERAL EDEMA Swelling of the ankles appearing during the day and subsiding during the night is a characteristic feature of right ventricular decompensation A considerable quantity of fluid must accumulate in the interstitial spaces before it becomes manifest as edema The edema which occurs with congestive heart failure is generally most severe in dependent regions particularly the lower extremities Digital pressure over such edematous regions displaces fluid and leaves a depression which persists for a few minutes (pitting edema) The skin becomes thickened and

waterlogged, as illustrated by a specimen from a patient who died with severe congestive heart failure (Fig 5) The soft tissues of the genitalia are particularly prone to develop edema Skeletal muscle fibers which are normally packed closely together are forced apart by the accumulation of edema fluid in the connective tissue stroma (Fig 5) In bedridden patients with advanced right ventricular failure, edema is often most prominent over the sacrum, which is the most dependent region in the supine position

EFFUSION INTO SEROUS CAVITIES Advanced stages of right ventricular failure in some patients are associated with the accumulation of fluid within the peritoneal cavity (ascites), within the pleural cavity (hydrothorax) and within the pericardium (hydropericardium)

Ascites may produce no signs or symptoms other than an increased abdominal girth, and may pass unnoticed The extent of ascites apparently correlates more with the pressures in the portal circulation than with the cardiac status A large proportion of patients with severe heart disease develop peripheral edema without demonstrable peritoneal effusion In contrast, patients with stenosis of the tricuspid valve or constrictive pericarditis often have severe ascites and mild peripheral edema No satisfactory explanation has been offered for the poor correlation between the severity of edema and of ascites Perhaps the mechanisms underlying the two conditions are different, since subcutaneous edema fluid usually contains less than 0 5 per cent protein while ascitic fluid contains protein in concentrations approaching that of plasma (5 to 6 per cent) The etiology of ascites has been reviewed recently by Hyatt and Smith[21] Extensive ascites is frequently associated with cirrhosis of the liver On this basis, ascites has been attributed to the escape of liver lymph into the peritoneal cavity, but reasons for such a phenomenon have never been clearly expressed

Pleural effusion occurs most commonly in patients with combined right and left ventricular failure Bedford and Lovibond[2] cited cases with isolated left ventricular failure and pleural effusion to support their concept that the transudation comes from the capillaries in the visceral pleura which drain into the pulmonary veins They expressed their belief that elevated pressure in pulmonary veins is a major cause of hydrothorax in such patients The observation that hydrothorax occurs more frequently in the right pleural space than in the left has never been satisfactorily explained

Pericardial effusion from congestive heart failure is rarely extensive or significant

ETIOLOGY OF PERIPHERAL EDEMA AND EFFUSION

Peripheral edema and effusion into serous cavities represent the accumulation of extravascular fluid, which has previously

TABLE 2 A PHYSIOLOGIC CLASSIFICATION OF EDEMA

Effective capillary pressure ↑	Capillary pressure ↑ (backward failure)
	Tissue pressure ↓
Effective plasma colloid osmotic pressure ↓	Plasma colloid osmotic pressure ↓
	Tissue colloid osmotic pressure ↑
Lymphatic drainage ↓	
Renal excretion of salt and water ↓ (forward failure)	

been attributed to a number of factors, including (a) increased effective capillary pressure associated with elevated venous pressure (b) reduced effective colloid osmotic pressure of the blood from abnormally increased capillary permeability (c) interference with lymphatic drainage and (d) selective retention of water and electrolytes by the kidneys (Table 2) Theories based on each of these factors have been discarded or criticized For example, capillary and venous pressures normally become greatly elevated in dependent extremities without edema formation evidence for increased capillary permeability has not been convincing causes of impaired lymphatic drainage have not been elucidated and mechanisms underlying renal retention of salt and water have been controversial Starling[23] recognized that no single etiologic factor was responsible for the formation of edema This mechanism which affects capillary filtration hydration of tissues lymphatic drainage and fluid balance deserves consideration

Increased Effective Capillary Pressure

Patients with advanced heart disease who develop obvious subcutaneous edema generally have elevated peripheral and central venous pressures Since the pressure in the capillaries must exceed the corresponding venous pressure to promote onward flow of blood the capillary pressures must be similarly increased Fluid balance at the capillaries is precarious because the osmotic attraction of plasma proteins is relatively fixed at values near the normal average capillary pressure These facts suggest a very plausible explanation for the development of edema and effusions as a result of increased capillary pressure Indeed Fahr and Ershler[4] directly measured capillary pressure in humans and reported that a generalized increase in capillary pressure of 8 mm Hg was consistently associated with demonstrable edema The severity of the edema was correlated with the height of the venous pressure Since the subcutaneous pressure is not significantly altered in the presence of edema tissue pressure plays no obvious role in producing increased capillary filtration Thus the relationship between elevated venous pressure and the development of edema and effusions leads to an attractive hypothesis namely, that edema is caused by increased capillary pressure This concept has recently been subjected to serious criticism (see *Backward Failure* p 152)

Reduced Effective Plasma Colloid Osmotic Pressure

An increase in capillary permeability allows greater quantities of protein to escape into the tissues diminishing the effective plasma colloid osmotic pressure (see Fig 12, Chapter 2) However evidence of increased capillary permeability in patients with congestive heart failure is tenuous and remains questionable The concentration of plasma proteins is not diminished in patients developing congestive failure The edema fluid in subcutaneous tissues contains less than 0 5 per cent protein On the other hand the concentration of protein in ascitic fluid and pleural effusions ranges between 3 and 6 per cent Lymph from these areas normally contains similar concentrations of proteins so increased capillary permeability is probably not a factor

Lymphatic Drainage

In the normal dependent extremity capillary pressure increases a great deal more than 8 mm Hg reaching levels ten times higher (80 or 90 mm Hg) at the ankle (Fig 2 Chapter 3) Indeed pressures in all subcutaneous veins more than 11 cm below the heart are more than 8 mm Hg greater than those in the veins at heart level Even during walking the venous pressure at the ankle remains higher than the maximum effective colloid osmotic pressure and capillary pressure exceeds this value Unless extravascular pressure is much higher than has been generally reported filtration occurs in the dependent extremities to the virtual exclusion of reabsorption of fluid into the blood The excess filtrate formed under these

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sheath[34 35] According to Chambers and Zweifach[36] the presence of a relatively stiff layer of material against the outer surface of the capillary endothelium is evident when a leukocyte passes outward through the capillary wall The extruded portion of the cell never moves directly away from the wall but spreads over the outer surface of the endothelium and remains for some time pressed closely between it and the pericapillary sheath The cell finally works its way through the interstices of the sheath to move more freely in the less resistant regions of the connective tissue matrix The pericapillary sheath appears to give mechanical support to capillaries Hyaluronidase applied to the frog mesentery abruptly produced microscopic petechial hemorrhages when liquefaction of the gels extended to the capillaries softening the supporting connective tissue sheath[36] It has long been recognized that increased permeability of capillaries may occur without increased fragility (characterized by the rupture of capillaries with the formation of petechial hemorrhages) It has been suggested that the capillary endothelium is responsible for permeability while the condition of the perivascular membrane determines the degree of capillary fragility The nature and organization of the interstitial spaces and gelatinous ground substance have important bearing on lymphatic function

The Lymphatic System Lymphatic collecting vessels tend to travel in close anatomic relation to the veins and have a similar function i e the return of blood elements from the tissues to the venous reservoirs near the heart (Fig 6) Further the lymphatic and venous systems both have superficial and deep distributions On the surface of the body the *superficial* lymphatic collecting vessels usually accompany the superficial veins just beneath the skin They also lie just beneath the mucous membrane throughout the whole length of the digestive respiratory and genitourinary tracts These networks of collecting lymphatics drain lymphatic capillaries abundantly distributed in the submucosa and in the dermis of the skin forming a continuous network throughout all the internal and external linings of the body except for the cornea of the eye

The *deep* lymphatic vessels intertwine and anastomose around the veins which accompany the deep arteries in their regional distribution to the organs of the body (Fig 6) Arteries veins, and deep lymphatics tend to share the same sheaths and are distributed to the same tissues and organs

The lymphatic system has two transport functions (*a*) the return of capillary filtrate back to the circulation and (*b*) the removal of foreign particles and exudates from tissue spaces and serous cavities Since the lymphatic capillary networks are distributed through the interstitial spaces along with the blood capillaries, the terminal vessels of the two systems must lie in close proximity (Fig 6) Most commonly, the lymphatic capillaries are believed to end blindly in interstitial spaces at varying distances from the capillaries of the blood vascular system There is also evidence that lymphatic capillaries may develop along the perivascular spaces where there appears to be less impedance to growth Lymphatic vessels which terminate within the pericapillary spaces are ideally located for the transportation of filtrate from the capillary beds Lymphatics lying free within the interstitial spaces may remove foreign particles and inflammatory exudates Under certain conditions, apertures have been observed in lymphatic capillaries which are surrounded by inflammatory exudate[37] When the tissues have been cleared of free fluid the lymphatic capillaries have continuous unbroken endothelial membranes

There are many gaps in our knowledge of lymphatic function The forces driving a fluid laden with protein and cellular elements through the continuous wall of a lymphatic capillary have not been clearly elucidated This problem is most acute in the skin of a dependent extremity where vascular pressures *are* very high and the

conditions is returned to the heart by way of the lymphatic system Since the lymphatic vessels appear to drain fluid from the interstitial spaces, it becomes important to visualize the characteristics of interstitial spaces

THE INTERSTITIAL SPACES In all tissues, the interstitial spaces are occupied by some form of connective tissue stroma which is traversed by the terminal branches and capillary networks of the vascular system (see Fig 2, Chapter 5) *The nature and extent* of this connective tissue varies from one organ to another In some tissues, the cells *are tightly packed so that the intercellular* spaces are not visible (e g , skeletal muscle, Fig 5) In other regions, the cells are widely *distributed throughout loose* areolar connective tissue (e g , subcutaneous tissue) It is now becoming clear that the spaces between cells are not occupied by "tissue fluid" in the usual sense, but rather by a gelatinous matrix composed of long chain polysaccharid-protein combinations (hyaluronates) organized into a lattice work[25 29] The water which is dispersed through such a gel does not flow as a free fluid in response to pressure gradients, it does not gravitate to dependent parts, and it cannot be withdrawn through a hypodermic needle thrust into the tissue spaces Water or physiologic saline injected into loose connective tissue becomes localized in the form of an edematous tumor On the other hand, substances such as alcohol, chloroform, or xylol disperse readily and do not accumulate around the point of injection[30] Water is held by hydrophilic properties of the gel in the connective tissue matrix Even when the subcutaneous tissues are waterlogged by massive edema, incision of the skin exposes a pearly gray surface from which water does not flow spontaneously, but a blotting paper placed in contact with this fully hydrated gel rapidly becomes soaked The physical characteristics of such a gel can influence the water content of tissues According to Lloyd and Phillips[31] the molecules of an organized protein can approach as closely as the length of their side chains permits At the isoelectric point, the molecules tend to be drawn together by electrostatic attraction which will favor the greatest degree of packing and hence the lowest degree of hydration On either side of the isoelectric point, *adjacent protein* molecules mutually repel each other By this means, the spaces between the molecules *in an organized protein are increased, leading* to an increase in the amount of water which can enter freely between the individual *molecules*

It has been shown that connective tissues swell when exposed to a 0 125 molar solu*tion of sodium chloride, and that the degree* of swelling increases greatly if the concentration is increased to 0 25 M (1 46 per cent)[32] *These values* lie on either side of a solution which is isotonic with the cells of the body Theoretically, edema would be promoted and increased by salt concentration in the interstitial gels of the body

The gelatinous "ground substance' gradually polymerizes, beginning shortly after birth, and tends to become progressively dehydrated with advancing age However, many factors may acutely alter the viscosity and hydrophilic character of this gel For example, enzyme systems (hyaluronidase) liquefy the gel by dissociating the long chain molecules These have been called "spreading factors" because they accelerate the dispersion of dyes or saline solutions injected into the subcutaneous connective tissues[33] The gelatinous state of interstitial spaces may have direct bearing on the exchange of fluid between tissues and capillaries

In contrast with the gelatinous matrix in the connective tissue spaces, a layer of free fluid surrounds the capillaries within the so-called 'perivascular space (Fig 6) This space is separated from the interstitial gel by the "perivascular membrane,' which consists of a fairly dense reticular fiber network enmeshing plate-like cells (*pericytes*) *The* pericytes, which resemble endothelial cells, lie between lamellae of the reticular fiber membrane *The investment by pericytes is* so complete that most of the capillaries are completely enclosed by a pericapillary

central venous pressure is increased the pressure against outflow from the lymphatic system is also higher and the average capillary pressures throughout the body are similarly increased Such a situation may upset the balance between filtration of fluid and elimination of filtrate by the lymphatic system

With some hesitation I am going to summarize briefly some thoughts which have repeatedly come to mind during the past seven years regarding the relation of lymphatic function to the fluid exchange across the capillary walls Very large differences between the capillary pressures and the tissue pressure in dependent extremities have been mentioned in the foregoing discussion (see also Chapter 3) In this connection it was suggested that the pressures outside the capillaries might be greater than have been generally recorded If the perivascular membrane reinforces capillary walls it must be capable of supporting a pressure The pressure within the perivascular membrane may exceed the pressure in the interstitial spaces The effective capillary pressure would correspond to the difference between the capillary pressure and the pressure inside the perivascular sheath The vertical height of the deep lymphatic channels is precisely the same as that of the corresponding veins (Fig 6) They are exposed to the same external conditions and pumping action since they travel together If the lymphatic pressure and the perivascular fluid pressure about the capillaries were similar to the venous pressure at all levels in the body the fluid balance at the capillaries would conform precisely with Starling s hypothesis in all areas as it does within the cerebrospinal cavity (see Fig 10 Chapter 3)

In two different sets of unreported experiments by M S McDonald and by M P Mullen the pressures in veins and in adjacent lymphatics have not been equal as would be expected from this analysis While venous obstruction regularly produced elevation in lymphatic pressure this increase was never as great as the increase in venous pressure However, lymphatic pressure always attained considerably higher levels than tissue pressure If the pressure in lymphatics reflects the pressure in perivascular spaces, the pressure immediately outside the capillaries is significantly greater than the tissue pressure measured by the usual technique (see Fig 1, Chapter 10)

The anatomic arrangement illustrated in Figure 7 should facilitate the entrance of capillary filtrate into the lymphatic capillaries without its passing through tissue spaces In the first place, the only free fluid outside the blood vessels is in the perivascular spaces and in the lymphatics If capillary filtrate can pass from the peri-

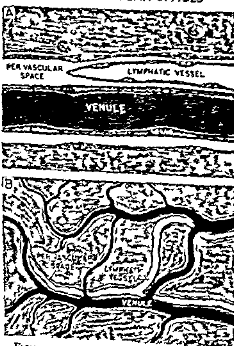


FIGURE 7 *A* Lymphatic capillaries tend to grow alongside veins within the perivascular space It is interesting to compare this relationship to the early concepts illustrated schematically by Sabin (see Drinker C. K. Lane Medical Lectures The Lymphatic System. Stanford University California Stanford University Press 1942 p 63)

B The perivascular spaces are visible only when they are distended with fluid in living tissues The perivascular membranes appear to be continuous with the connective tissue sheath enclosing veins (Drawn from photomicrographs presented by Clark and Clark 33)

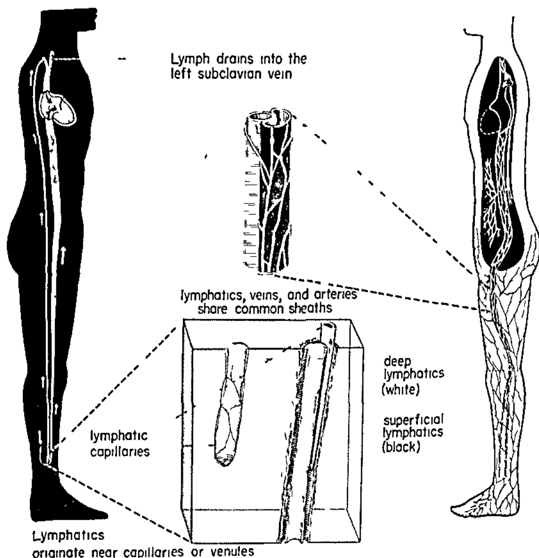


FIGURE 6 The lymphatic system is essentially a paravenous system since the lymphatic capillaries lie in close association with the capillaries and veins of the blood vascular system the collecting lymphatics tend to accompany veins and arteries and drain into the central veins Like the veins the lymphatic system consists of both deep and superficial distributions of vessels and carries constituents of the blood back to the region of the heart

tissue pressures very low The exact mechanisms elevating lymph from dependent extremities to the level of the subclavian vein are not universally agreed upon, although a number of possibilities exist The lymphatic collecting vessels are intimately associated with the veins and are subject to the same muscular and abdominothoracic pumping actions (see Chapter 3) Confined within the same sheath as arteries and veins, the lymphatics would tend to be compressed by changes in the caliber of these vessels Even the arterial pulse may act as an accessory pump, displacing lymph upward with each wave of distention Finally, there is some evidence that certain lymphatics have independent contractility which theoretically could propel lymph by a peristaltic type of action

The lymphatic pressure in the thoracic duct must exceed the pressure in the subclavian veins into which it empties If the

Both the strength and the weakness of this concept lie in the fact that it is a functional interpretation of the pathologic changes in patients dying from heart failure. Certainly, the pathologic picture of congestion "looks" like the result of damming of blood behind a failing chamber (Figs. 1 and 6). However, a number of discordant factors can be marshalled against this concept.

If blood is dammed up behind the right ventricle, where does all this blood come from? Referring to the hydraulic model in Figure 3, it seems clear that a failure of the pump on the left would accumulate fluid in the large reservoir upstream only by evacuating the blood from the smaller (pulmonary) reservoir. Generalized systemic and pulmonary congestion implies a marked increase in total blood volumes (renal retention of fluids). If increased renal venous pressure produces renal retention of salt and water, how did the renal venous pressure become elevated in the first place?

Burch and Ray[38] reviewed some of the observations which are incompatible with the backward failure theory. For example, venous hypertension is known to exist in clinical states with little or no edema, e.g., therapeutic ligation of the inferior vena cava.[39] The capillary pressures in the dependent extremities of normal individuals are much higher than the elevated central venous pressure during congestive heart failure. Systemic venous congestion and edema do not appear even after destruction of practically all the right ventricular musculature either in experimental animals[40, 41] or in patients with extensive right ventricular infarction.[4]

Therapeutic procedures such as a low salt diet or the administration of mercurial diuretics promote disappearance of edema, decline in venous pressure and reduction in the size of the liver, but have no known direct effect on the heart. A syndrome very similar to congestive heart failure can be produced by excessive administration of desoxycorticosterone acetate, which is not supposed to affect the heart significantly. A similar syndrome occurs when large amounts of water and electrolytes are administered to patients with anuria due to renal disease. Recognition of such deficiencies has led many investigators to favor the forward failure theory.

The Concept of Forward Failure

Advocates of this theory attribute the formation of edema to diminished cardiac output. The forward failure theory antedated the backward failure theory but was not widely accepted for many years. Originally, the diminished cardiac output was believed to produce peripheral constriction and anoxia, which increased capillary permeability and thus produced transudation of fluid into the tissue spaces. However, the capillary endothelium is in direct contact with the blood. *If these cells are sufficiently anoxic to increase capillary permeability, what must be the state of the cells at some distance from the capillaries?* Neither venous congestion nor edema is characteristically produced by severe anoxia resulting from pulmonary disease, cyanotic congenital heart disease or living at high altitude. However, more recently cardiac catheterization has provided direct evidence of abnormally low cardiac output in many patients with advanced heart failure. Reduction in renal blood flow of such patients has also been demonstrated (see Fig. 1, Chapter 8). Thus, the diminished cardiac output is now supposed to lead to a diminished renal blood flow and the retention of salt and water. Particularly damaging arguments result from observations that urinary output does not correlate well with renal blood flow, and that control of urine volume is vested primarily in the extent of tubular reabsorption. The kidney actually expends more energy in reabsorbing salt and water than in excreting large urine volumes with a specific gravity of about 1.010. The connection between cardiac output and renal tubular function has not been established.

For these reasons, I would like to see both the forward and the backward failure

vascular space directly into lymphatic capillaries confined within the perivascular sheath, this mechanism for the formation of lymph would explain the passage of protein, blood cellular elements, bacteria, dyes, etc into the lymphatic system Clark and Clark[35] reported observing blood cells passing directly from capillaries into adjacent lymphatic vessels, but they do not feel that this is a typical or a functionally significant phenomenon While considerable circumstantial evidence can be advanced to support the concept summarized above, it remains completely unsupported by direct experimental measurements and must be treated purely as an interesting armchair theory

The mechanism described above resembles a concept held by von Recklinghausen based on his belief that lymphatic capillaries open directly into the tissue spaces This concept was discarded after it was generally agreed that lymphatic vessels possess an unbroken endothelial lining In view of the difficulty involved in studying lymphatic function, the anatomy and function of these apparently simple vessels still hold mysteries which are currently unsuspected

Renal Retention of Salt and Water

One glaring omission from the previous discussion of edema is the source of the accumulated extracellular fluid Patients developing congestive failure and peripheral edema gain weight because the amount of body fluid increases Similarly, a generalized systemic venous congestion implies an increased total blood volume This additional fluid in the form of blood, edema and effusion must accumulate as a result of either greater fluid intake or incomplete excretion Ample evidence now indicates changes in the control of blood and fluid volumes of the body which are very important in promoting this condition, these mechanisms will be considered in more detail below

Recognition of the important role played by renal dysfunction in the development of venous congestion and edema has brought into sharp relief a most unfortunate controversy between proponents of two theories concerning the etiology of congestive heart failure the backward failure and forward failure theories Mention of these two concepts has been studiously avoided on the basis that they have channeled thought and investigative effort along relatively fruitless lines To me this controversy is comparable to a debate among police officers concerning the relative seriousness of embezzlement and burglary sustained to the point that effective investigation of suspects is neglected

The Concept of Backward Failure

According to the backward failure theory, the failing ventricle becomes distended and loses contractile power To maintain the required cardiac output the diastolic filling pressure rises, increasing the stroke volume in accordance with Starling's law of the heart If the ventricular distention exceeds some critical value, further increase in ventricular filling pressure reduces ventricular output The increased diastolic pressure in the left ventricle elevates the pressures throughout the venous and capillary channels upstream from the failing chamber The increased venous pressure is attained by venous engorgement as though the blood were dammed up behind an obstruction in a flowing stream This idea is sometimes expressed as "the ventricle is unable to eject the quantity of blood which comes to it," although I have no clear picture of what that phrase means in a closed circuit The generalized increase in venous and capillary pressures augments filtration through the capillary walls so that fluid tends to collect in the interstitial spaces Fluid lost into the interstitial spaces is replaced by increased fluid intake or by adjustment in renal output so edema and effusion of fluid continue until a new equilibrium is established In response to recent emphasis on the importance of renal retention of salt and water, proponents of this idea have presented evidence that elevated renal venous pressure produces a diminution in urine output

regulating system generalized venous congestion and peripheral edema would represent changes in the operating level of the controls regulating blood volume and total body fluids Unfortunately we have no clear picture of this regulatory mechanism The integrating mechanisms are similarly in doubt and our data concerning the regulation of fluid intake in response to thirst drive and the control of salt and water reabsorption in the kidney are fragmentary

MECHANISMS FOR MONITORING TOTAL BLOOD VOLUME. Monitoring systems responding to changes in blood volume are most likely to be situated in the walls of the intrathoracic venous channels including the atria (see Chapter 5) For a long time sensory fibers responding to distention of these channels have been postulated to serve the Bainbridge and McDowall reflexes There is evidence[50] that receptors in the thoracic viscera detect changes in blood volume and induce appropriate changes in the peripheral vascular bed and in renal function Distention of intrathoracic vascular channels induced artificially by negative pressure breathing leads to an increase in urine flow averaging 350 per cent in man[51] Boucek et al[1] demonstrated that pulmonary congestion produced by constricting pulmonary veins with cellophane bands induced increased blood volume without increased systemic venous pressure or ascites In contrast obstructing outflow from the systemic veins produced elevated systemic venous pressure ascites and peripheral edema These observations suggest that a volume-monitoring system lies somewhere in the thorax The effector mechanisms for blood volume control would presumably adjust intake and elimination of fluids electrolytes and other constituents requiring integration by complex nervous and hormonal systems The mechanisms which normally control volumes of blood and body fluids must be adjusted to an abnormally high level during congestive heart failure

MECHANISMS FOR CONTROLLING TOTAL BODY FLUIDS The partitioning of fluid between the intracellular and extracellular compartments is determined primarily by the maintenance of osmotic equilibrium The tremendous potential osmotic forces illustrated by Figure 11 in Chapter 2 assure equal osmotic concentration throughout the body except across semipermeable membranes (endothelial barriers) According to Verney[53] osmoreceptors in the hypothalamus monitor the osmotic pressure of the blood (and extracellular fluid) and institute appropriate adjustments in renal output Such a control may aid in maintaining the total osmolarity of body fluids However there is no obvious means by which such receptors could be affected by an increase in the total amount of isotonic body fluids as occurs in edema

The current methods of treating congestive heart failure are directed toward improving cardiac efficiency and reducing total body fluids toward normal levels These techniques are used primarily because they have been shown to be effective Therapeutic techniques which unquestionably improve the conditions of patients are useful whether they can be adequately explained or not Elucidation of the normal regulation of total blood and fluid content of the body and the aberrations produced by disease should result in improved methods of treatment in the future Recognition of the deficiencies in current knowledge by investigators and clinicians alike represents the first big step toward clarifying these issues

SUMMARY

Left ventricular failure is characterized by symptoms resulting from pulmonary congestion induced by elevated filling pressures in the ventricular chamber The most prominent symptom is dyspnea which apparently results from reflexes associated with distention of pulmonary veins and the left atrium and from increased respiratory effort due to rigidity of a congested and indurated pulmonary parenchyma Congestion of the bronchial mucosa is associated with pulmonary congestion because the capillary

theories discarded to avoid the semantics and the emotional connotations involved If this happened, more attention could be directed toward the mechanisms controlling blood volume and total body fluid I tend to agree with Elkington and Squires,[43] who stated "The absolute level of cardiac output does not correlate with the degree of edema, and cannot explain it on either a 'backward' or 'forward failure' theory An output of the heart which is inadequate in relation to metabolic demands would appear to be a primary factor leading to secondary changes in circulatory dynamics in several regions of the body Renal retention of salt and water results from more than circulatory disturbance causing a diminished glomerular filtration, tubular transfers are involved and these are conditioned by humoral and cellular, as well as by circulatory factors In short, the homeostatic mechanisms which control body fluid volume unknown in part, may be functioning in an abnormal way in congestive failure"

Control of Blood Volume and of Total Body Fluids

The blood volume and total fluid content of normal individuals remains remarkably constant in spite of wide variations in fluid intake, fluid loss dietary habits etc So long as the volume of fluid in the various compartments remains relatively fixed and the concentration of each constituent is maintained within a narrow range, the total quantity of each constituent in the body remains remarkably constant Although selective excretion and retention by the kidneys is extremely important, the intake of food and fluid is also rather precisely regulated For example, Adolph[44 45] demonstrated that dogs deprived of water for varying periods of time make up the deficits with extraordinary precision within two or three minutes, and then become disinterested in further drinking Thus, enough fluid to restore normal fluid content is drunk before any significant portion of the fluid is absorbed from the gastro-intestinal tract The rate at which the dogs ingested water was approximately proportional to the water deficit even when the fluid escaped from esophageal fistuli and never entered the stomach The quantity of fluid passing through the pharynx and to the outside was closely related to the water deficit Bellows[46] reported that the temporary satisfaction secured by the passage of water through the mouth and pharynx is superseded by a delayed and more prolonged satisfaction when the fluid reaches the lower portions of the gut Gilman[47] has suggested that the stimulus to thirst depends upon the water content of the cells, which is affected by the osmotic concentration of body fluids Bare[48] demonstrated that adrenalectomized rats selectively imbibed greater quantities of salt than normal rats Richter[49] reviewed a wide variety of evidence that alterations in the internal environment due to nutritional and endocrine factors tend to be countered by appropriate selection of specific substances in animals, infants children and adult humans Thus, the maintenance of relatively constant body weight, blood volume and total fluid content of the body with but slight variability in the concentration of the various components involves exceedingly complex mechanisms regulating both intake and output of many different substances

Control of blood volume implies the existence of receptors which continuously monitor the quantity of blood on the venous side of the circulation There must also be an integrating system by which stimuli from various sites produce appropriate responses by the effector mechanisms directly or indirectly adjusting the intake, output, production and disposal of all the constituents of the body fluids A corresponding system for the regulation of the arterial blood pressure consists of pressoreceptors integrating centers in the central nervous system and effectors of wide variety including both neural and chemical influences on peripheral resistance and cardiac activity Just as systemic arterial hypertension represents a readjustment in the level of operation of this

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networks of both systems drain by way of the pulmonary veins Congestion and edema of the membranous lining of the airways increases *the resistance to the airflow in and* out of the alveoli Secretion of mucus causes a productive cough Extravasation of blood from the bronchial capillaries, and possibly into alveolar sacs, may produce blood-tinged sputum (hemoptysis) Vague symptoms such as fatigue, gastro-intestinal disturbance and renal dysfunction may be attributed in part to restricted cardiac output

Right ventricular failure produces generalized systemic venous congestion associated with increased central venous pressure Cyanosis may result from a combination of retarded blood flow through the skin and the associated pulmonary congestion and edema from concomitant left ventricular failure Peripheral edema consists of accumulation of fluid in the interstitial spaces, first appearing in dependent extremities (ankles) and later advancing up the legs and frequently involving the genitalia Such subcutaneous fluid contains protein in concentrations less than 0 5 per cent Effusions in the serous cavities (ascites, pleural and pericardial effusions) represent extravasation of fluid containing protein in considerable quantities (3 to 6 per cent) The causes of edema can be classified according to the fac*tors implicit in Starling's hypotheses of* fluid exchange at the capillaries Of these, the most important would appear to be increased capillary pressure due to the elevated venous pressure Edema cannot form so long as the lymphatic system is capable of draining the excess filtrate For this reason the *structure and function of the lymphatic* capillaries deserve consideration Of even more importance is the fact that generalized venous congestion, peripheral edema and effusion into serous cavities cannot occur unless the total quantity of body fluids increases In this sense, the renal retention of salt and water must play an important role in the development of congestive failure

In the past, two concepts have been employed to explain the origin of congestive failure Advocates of the backward failure theory suggest that blood is dammed up behind the failing ventricle, elevating venous pressure, promoting venous congestion and producing peripheral edema through elevated capillary pressure The *same changes* were originally attributed to diminished cardiac output (forward failure), anoxia of peripheral vessels, increased capillary permeability and escape of fluids into the tissues More recently restricted cardiac output has been assigned a role in causing abnormal re*tention of salt and water which expands* blood volume as well as promoting edema Serious discrepancies are apparent in both theories It would seem profitable to investigate the normal mechanisms for monitoring and controlling both the total blood volume and total body fluids On this basis the *aberrations produced by cardiac* disease might be more clearly understood

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Part Four

METHODS OF CARDIAC DIAGNOSIS

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Part Four

METHODS OF CARDIAC DIAGNOSIS

Introduction to Part Four

Recognition of heart disease after signs of right or left ventricular failure have become evident is of limited benefit to either the physician or his patient The opportunities for remedial therapy have been largely forfeited by the time the patient reaches this phase of his disease The ultimate goal of clinical diagnosis is the detection of disease at the earliest possible moment so that adequate therapy can be instituted Recognition of early manifestation of cardiovascular disease requires a constant search for subtle clues which herald the development of organic cardiovascular disease These clues may be elicited in the course of careful questioning of the patient, physical examination or laboratory tests Rapid technologic advances have increased the number of methods for routine evaluation of cardiac function to serve as supplementary sources of clues

The next six chapters are devoted to a consideration of various methods which can be profitably used to facilitate detection and interpretation of cardiac disease In spite of a rapidly expanding diagnostic armamentarium, most of the essential information for a complete functional analysis of the heart is not available A physician can be compared to a hydraulics engineer who is required to examine a defective pump without exposing the mechanism, and to make all repairs without replacing damaged parts and without interrupting the activity of the mechanism In general, both the hydraulics engineer and the physician are obliged to await the appearance of signs of dysfunction, diagnose the difficulty and attempt to restore the mechanism to the best of their ability Since the onset of cardiac malfunction is insidious, the challenge lies in detecting disorders before irreparable damage has occurred

Chapter 10

Pressure Measurements

The three principal attributes of circulating blood are (a) flow (b) volume and (c) pressure Various methods for measuring cardiac output (see Chapter 12) provide information concerning total blood flow through the heart. However no technique for computing blood flow through either the human heart or the peripheral circulation yields what can be regarded as direct measurements Similarly the volume of internal organs can be estimated from roentgenographic silhouettes but there is no method for directly recording the absolute volume Thus of the three important variables in the circulation only blood pressure can be directly measured in patients By means of hypodermic needles and catheters intra vascular pressures in virtually all portions of the human cardiovascular system have been intensively studied and many ingenious pressure recording devices have been developed for these purposes

Measurements of pressure have been widely misinterpreted as indicative of variations in volume and flow For example increased venous pressure has been said to indicate increased volume of blood in the veins increased effective filling pressure and increased diastolic volume of the ventricles Whenever a change in volume is postulated solely from a change in pressure potential variations in the distensibility of the veins cardiac walls or arteries are tacitly overlooked or denied Such a practice is extremely misleading since active changes in the caliber or changes in distensibility are known to occur in every category of vessel in which they have been sought with the possible exception of the capillaries themselves Therefore changes in the pressure within the circulatory system are not reliable indicators of its capacity or volume

The difference between the pressures at two points in the circulatory system has been frequently employed to predict changes in blood flow Changes in the pressure gradient along a series of vessels will produce corresponding changes in blood flow only if the resistance to flow between the two sites of measurement remains unchanged The resistance to flow can be determined only by simultaneously measuring both the pressure gradient and the blood flow

Attempts to describe the flow volume and pressure in the circulatory system by measuring only the pressure correspond to attempts to analyze the functional characteristics of a television set by using only a voltmeter Nonetheless direct pressure measurements have intrinsic value in determining certain of the conditions under which the circulatory system is functioning

MEASUREMENT OF STATIC PRESSURES

A vertical column of fluid in a manometer and an accurate ruler are the only tools needed for measuring steady pressures It is well to remember that even the most intricate pressure measuring devices require calibration by such simple pressure indicators Thus the fluid manometer is the basic instrument for pressure recording and for many applications may be preferable to the expensive complicated and insensitive electronic pressure transducers which are now in vogue

Peripheral Venous Pressure

The venous pressure can be measured by a needle connected through a three way

MEASUREMENT OF PERIPHERAL VENOUS PRESSURE

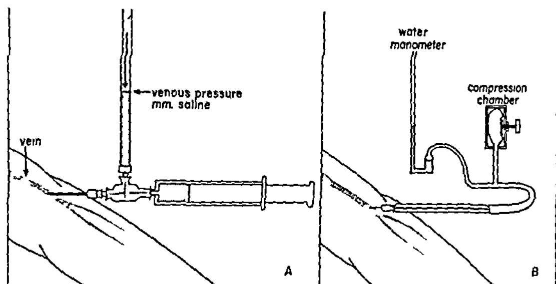


FIGURE 1 *A* Venous pressure can be measured by a simple vertical manometer filled with saline and connected to a needle which has been thrust into a vein The fluid column in the vertical tube descends until its pressure is in equilibrium with venous pressure at the point of measurement

B The phlebomanometer of Burch and Winsor[1] consists of a small hypodermic needle fastened to a glass capillary partially filled with sterile fluid The remainder of the system except the water manometer is filled with air The manometer registers the pressure in the system as adjusted by twisting the screw on the compression chamber until the fluid in the glass capillary is stationary The pressure in the water manometer then indicates venous pressure when corrected for capillary and hydrostatic pressures in the needle and observation tubing

stopcock to a vertical manometer From the syringe, sterile saline is expressed into the manometer to a level above the possible venous pressure (Fig 1*A*) The valve on the stopcock is then turned so the vertical tube becomes continuous with the needle The saline runs into the vein until the vertical height of the column of saline is in equilibrium with the venous pressure at the point of the needle

Alternatively the phlebomanometer of Burch and Winsor[1] is well suited to measurement of pressure in both large and small peripheral veins (Fig 1*B*) In this apparatus, a small needle is fastened to a capillary tube which is connected by a rubber tube to a small air chamber the capacity of which can be adjusted to elevate the pressure in the system A water manometer indicates the air pressure within the tubes Sterile saline is drawn into the capillary tube until the meniscus lies at a reference line When the needle is inserted into a vein, the meniscus will move farther along the capillary tube if the venous pressure exceeds the pressure within the phlebomanometer By elevation of the pressure in the system, the meniscus can be brought to a standstill at the reference line when the pressure in the manometer equals the venous pressure A correction (about 20 mm H_2O) must be made for the capillarity of the needle and observation tube A more compact version of this instrument was recently described by Sodeman[2]

The average pressures in superficial veins measured in a large number of normal supine humans are illustrated in Figure 1, Chapter 3 The average venous pressure in small tributaries at the wrist and ankle attains levels of 139 to 188 mm H_2O (10 to 14 mm Hg) In all regions of the body, veins of corresponding size have similar pressures Individual values obtained from similar sites in different individuals varied as much as 100 mm H_2O However in each indi-

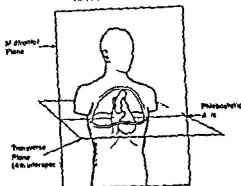
vidual a gradient in venous pressure from the distal portion of the extremities toward the heart was apparent

THE SIGNIFICANCE OF VENOUS PRESSURE The veins originate at the capillaries and terminate at the heart Thus venous pressure has important bearing on the function of both the capillaries and the heart The pressure in the smallest peripheral veins is a basis for deducing the minimal pressure in the capillaries of the region since the capillary pressure must exceed venous pressure The pressure in the large intrathoracic veins reflects the diastolic filling pressure of the ventricles

Right atrial pressure ranges just above or below atmospheric pressure but the pressure in extrathoracic veins is 2 to 5 cm H O higher A rather sudden drop in pressure often occurs as the veins penetrate the thoracic walls where the extravascular pressure becomes subatmospheric According to Duomarco et al [3] branches of the superior vena cava in normal erect subjects are collapsed from the point of entrance into the thorax to a level a few centimeters above the right atrium The sudden drop in pressure indicates local constriction at or near the point at which the veins pass through the thoracic musculature In any case the venous pressure in the arms does not normally reflect right ventricular diastolic pressure However if central venous pressure rises e g in congestive failure the difference between intrathoracic and extrathoracic venous pressure disappears and the brachial venous pressure becomes a fairly reliable indicator of central venous pressure

THE PHLEBOSTATIC LEVEL. To obtain comparable figures in different individuals or in a series of measurements the venous pressure is frequently measured at the level of the right atrium For this purpose Winsor and Burch[4] described a reference line (the phlebostatic axis) which passes transversely through the thorax midway between the anterior and posterior surfaces of the trunk at the level of the fourth interspace at the sternum (Fig 2A) The phlebostatic level is a horizontal plane at the level of the phlebostatic axis Venous pressures anywhere in the body can be measured as the vertical height of a fluid column above this plane (Fig 2B)

BASELINE FOR CENTRAL VENOUS PRESSURE



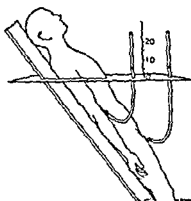


FIGURE 2 *A* The phlebostatic axis is defined as the line of junction between two planes (*a*) a mid frontal plane and (*b*) a plane at right angles passing through the junction of the fourth rib with the sternum. The phlebostatic axis passes through or near the mid-portion of the right atrial chamber

B The phlebostatic level is used as the zero reference for venous pressures measured in different locations with the body in various positions The phlebostatic level is a horizontal plane passing through the phlebostatic axis.

Extravascular Pressures

Water manometers are generally employed for measuring tissue pressures in various sites For example, pressures in the skin subcutaneous tissue and muscle have generally been recorded with apparatus resembling

the phlebomanometer (Fig 1*B*) Cerebrospinal fluid pressure is usually measured with simple vertical manometers of the type illustrated in Figure 1*A*

Since the pressures in veins and extravascular spaces rarely change abruptly they can be recorded quite accurately with simple fluid manometers However, such a manometer is entirely inadequate for recording pressures which fluctuate widely and rapidly, especially when the extremes of pressure are significant The inertia of the fluid and resistance to its flow into the manometer prevent the fluid level from following the rapid changes in pressure If a mercury manometer is connected directly to an artery through a hypodermic needle, the mercury column oscillates slightly above and below the mean pressure, which obviously does not reliably indicate the magnitude of either the systolic or the diastolic pressure The same problem arises in measuring the widely fluctuating pressures in the ventricular cavities Thus, more complicated apparatus is required to measure arterial and ventricular pressures accurately

MEASUREMENT OF ARTERIAL BLOOD PRESSURE

Measuring arterial blood pressure involves determining both the systolic and the diastolic pressures These two pressure levels actually represent the amplitude of the arterial pressure pulse at the point of measurement For this reason, the origin and characteristics of the arterial pulse wave deserve consideration

The Arterial Pulse

At the onset of ventricular ejection, blood flows into the aorta faster than it leaves through the arterioles The inertia of the long columns of blood in the arteries opposes acceleration Blood ejected by the left ventricle accumulates in the first portion of the aorta (Fig 3*A*), increasing the tension in the walls of this region The increased pressure and wall tension in the root of the aorta force blood into the adjacent segment of aorta which, in turn, is stretched and develops increased tension In this way, a pulse of pressure moves rapidly down the aorta at a velocity which is determined by the elasticity of the walls and the pressure of the blood (Fig 3*B*)

During the latter part of ventricular systole, blood leaves the arterial system by way of the arterioles faster than the rate at which it enters from the left ventricle, and the pressure in the root of the aorta falls Ventricular pressure drops rapidly to a level below the arterial pressure, and the aortic valves close Closing of the valves involves a retrograde flow of blood in the root of the aorta which produces a notch or incisura in the descending limb of pressure pulses recorded from this region

The arterial pulse is altered in its form as it passes rapidly through the arterial system[5,7] by pressure waves reflected from the peripheral arteries and arterioles, rebounding in a retrograde direction along the arterial tree This phenomenon produces standing waves of pressure in the descending aorta and peripheral arterial trunks These waves tend to augment the peak amplitude of the pulse wave, to obscure the incisura and to depress the trailing portions of the pulse wave However, they have little effect on the pulse wave in the arch of the aorta, and the pulse pressure is essentially undistorted in this region In the brachial artery, the standing waves produce an increase in the systolic peak and a slight reduction in the diastolic level, so that the arterial pulse pressure is greater in the arms than it is in the arch of the aorta In the arteries of the lower extremities, the reflected waves of pressure distort the pulse wave even more, so that the systolic pressure may be 15 to 25 mm Hg higher and the diastolic pressure a little lower than they are in the arms even with the subject reclining However, the mean arterial pressure (Fig 6) is slightly higher at the aortic arch than at the periphery The arterial pressure pulses in Figure

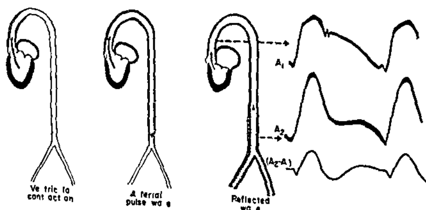
3*A* indicate schematically the changes in pulse contour as they are measured at various points along the arterial tree

Sphygmomanometry

Since the pulse waves rapidly spread through the arterial system and are modified to varying degrees by reflected waves it is apparent that at any instant the arterial pressure varies throughout the arterial tree Determinations of arterial pressure generally represent the maximal and minimal pressure of the pulse wave at the point of measurement.

The most accurate records of arterial pressure pulses are obtained through intraarterial needles connected to suitable pressure recording systems (*vide infra*) To reproduce the wave as it appears in the artery, the recording paper would have to move at the velocity at which the pulse travels past the needle (Fig 3*B*) Since this is impractical the records are generally obtained on paper moving relatively slowly, and the pulse waves are compressed in time (Fig 4)

The arterial blood pressure is generally measured with a sphygmomanometer consisting of an inelastic cuff containing an inflatable rubber bag The rubber bag is connected by rubber tubing to a rubber bulb



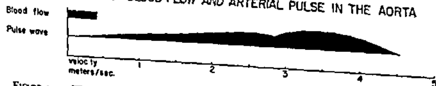


FIGURE 3 The arterial pressure pulse is a wave of pressure which passes rapidly along the arterial system Blood suddenly ejected into the ascending aorta at the beginning of systole has insufficient energy to overcome all of the inertia of the long columns of blood in the arteries Therefore blood tends to pile up and distend the ascending aorta causing a sudden local increase in pressure Blood is then forced into the next portion of the aorta, extending the region of distention and initiating a pulse of pressure which travels rapidly along the arteries toward the periphery These waves of pressure reflected by peripheral structures travel back toward the heart and become superimposed on the advancing pulse wave This produces a higher peak of systolic pressure a slurring of the incisura and a lower diastolic pressure in the femoral artery If the peripheral arterial pulse wave is subtracted from the pulse recorded at the arch of the aorta, the resulting wave form ($A_2 - A_1$) represents the reflected or standing waves in the distal portion of the arterial system The pulse wave velocity (4 to 5 m. per second) is much faster than the velocity of blood flow (less than 0 5 m. per second) The pulse wave velocity is determined by the elasticity of the arterial walls which in turn depends upon their distensibility in relation to the blood pressure

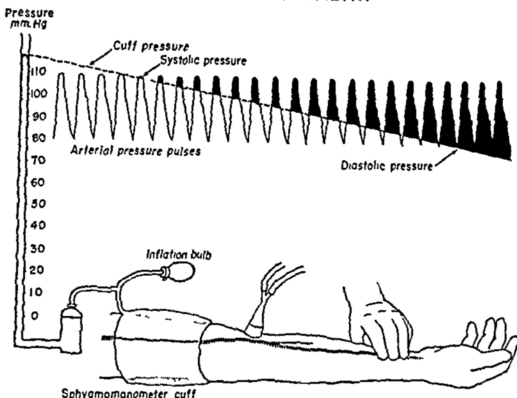


FIGURE 4 - When the pressure within the sphygmomanometer cuff is increased above arterial blood pressure the arteries under the cuff are occluded and no pulse can be palpated at the wrist As the cuff pressure is gradually released the systolic peaks of pressure finally exceed cuff pressure and blood spurts into the arteries below the cuff producing palpable pulses at the wrist The sudden acceleration of blood below the cuff produces vibrations which are audible through a stethoscope The pressure in the mercury manometer at the time the pulse is heard or felt indicates systolic pressure As cuff pressure is further diminished, the sounds increase in intensity and then rather suddenly become muffled at the level of diastolic pressure where the arteries remain open throughout the entire pulse wave At still lower pressures the sounds disappear completely when laminar flow is re-established

and to a device which continuously records the pressure within the cuff (e g a mercury manometer, Fig 4) When the cuff is snugly applied to the arm, inflation of the rubber bag compresses the tissues under the cuff If the rubber bag is inflated to a pressure which exceeds the peak of the arterial pulse wave, the artery is continuously collapsed and no pulse wave can be palpated in the artery peripheral to the occlusion If the pressure in the cuff is gradually reduced a point will be reached at which the peak of the pulse wave slightly exceeds the pressure in the surrounding tissues and in the rubber bag (Fig 4) At that level, the pulse becomes palpable and the pressure indicated on the mercury manometer is a measure of the peak of the arterial pulse or systolic pressure

The spurt of blood flowing through the artery under the cuff rapidly accelerates the column of blood in the peripheral arterial tree producing turbulence and distinctive sounds (Korotkoff sounds) which can be heard through a stethoscope applied over the artery just below the cuff [8] As the pressure in the cuff is reduced further the difference between systolic pressure and cuff pressure progressively widens and the artery is open during a greater proportion of the time In general the quantity of blood surging under the cuff is similarly increased and the sounds heard through the stethoscope tend to become louder When the pressure in the cuff falls below the minimal pressure of the arterial pulse wave, the artery remains open continuously and the emitted sounds

become muffled because the blood flows continuously and the degree of acceleration of the blood by the pulse wave is suddenly reduced. At still lower cuff pressures, the sounds disappear altogether as laminar flow is re-established.

The pressure at which the sounds become muffled has been generally accepted as the diastolic pressure. However, Bordley et al.[9,10] recently recommended that the cessation of sounds should be substituted for this established end point. This recommendation was termed a major setback to medical science by Burton[11] and compelling reasons for ignoring the proposal were presented in a most stimulating review.

SOURCES OF ERROR IN MEASURING ARTERIAL PRESSURE. Significant errors in arterial blood pressure readings result from improper selection or application of sphygmomanometer cuffs.[1,13] The pressure *which exists in the rubber bag* is transmitted to the greatest depth at the center of the cuff. If the cuff is sufficiently wide and is properly adjusted, the pressure indicated by the manometer extends to the tissues immediately surrounding the artery (Fig. 5A). However, if the limb is too thick in relation to the width of the cuff, the pressure around the artery may be significantly less than that recorded from the rubber bag (Fig. 5B). Under these conditions, the cuff pressure required to collapse the artery must exceed the pressure which exists in the artery at that point. Thus the systolic (and diastolic) pressure readings will be too high. If the cuff is loosely applied (Fig. 5C) so that the rubber bag must be partially inflated before it exerts pressure on the tissues, the area of contact is seriously reduced, corresponding to a very narrow cuff.

THE AUSCULTATORY GAP. In some patients, the sounds emitted from the artery below the cuff disappear over a fairly large range in pressure between the systolic and diastolic pressures. The cause of this auscultatory gap is not known. If the cuff pressure is increased only to levels within the range of the auscultatory gap, the systolic pressure may be noted at the lower end of this silent range and indicate a normal systolic pressure when, in fact, the true systolic pressure is excessively high. Since the pulse wave *persists in the range of the auscultatory gap,* this source of error can be eliminated by routinely checking systolic pressure by both the auscultatory and the palpatory methods (Fig. 4).

TRANSMISSION OF CUFF PRESSURES TO THE TISSUES OF THE ARM

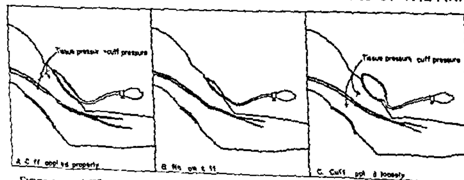


FIGURE 5. *A* When a sphygmomanometer cuff of sufficient width in relation to the *diameter* of the arm is properly applied, the tissue pressure around deep arteries under the cuff equals cuff pressure. However, pressure under the edge of the cuff does *not* penetrate as deeply as that under the center of the cuff.

B A cuff which is *too* narrow in relation to the diameter *of* the limb does not *transmit* its pressure to the center of the limb. Under these conditions, the cuff pressure must greatly exceed arterial pressure to produce complete occlusion of the artery, and erroneously high systolic and *diastolic pressures* will be read from the mercury manometer.

C If a cuff of sufficient width is applied *too* loosely, it becomes rounded before exerting pressure on the tissues and produces the same sort of *error* as a narrow cuff.

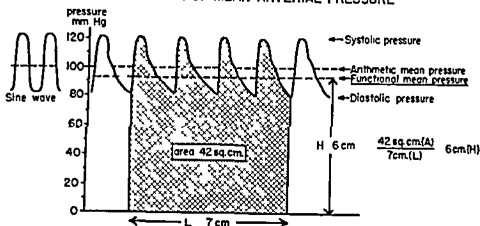


FIGURE 6 If the systolic pressure is 120 mm Hg and the diastolic pressure 80 mm Hg the arithmetic mean pressure is 100 mm Hg If the arterial pulse wave were symmetrical (a sine wave) this value would represent the average perfusion pressure However the interval during which the arterial pressure is less than 100 mm Hg is longer than that during which it is elevated above this level so the functional mean pressure is less than 100 mm Hg The functional mean pressure is determined by dividing the area of the shaded region (area = 42 sq cm) by the horizontal dimension (L = 7 cm) to determine the height of a rectangle having the same area (H = 6 cm) The functional mean pressure tends to be higher than diastolic pressure by about one-third the pulse pressure but this estimate does not apply to pulse waves having different contours e g with changes in heart rate

MEAN ARTERIAL BLOOD PRESSURE Since the arterial blood pressure fluctuates during each cardiac cycle, the mean arterial pressure is often used in clinical and experimental reports The arithmetic average of the systolic and diastolic pressures would provide an accurate indication of the mean arterial perfusion pressure only if the arterial pressure pulse were a sine wave (see Fig 6) However, the arterial pulse wave in no way resembles a sine wave and the arithmetic average of systolic and diastolic pressures is not an accurate expression of the mean pressure The true mean arterial pressure can be determined by damping out the pulses or by integrating the arterial pulse wave on accurate records of the pressure pulse Vertical lines are dropped from corresponding points on arterial pulse waves to the zero pressure line The arterial pressure pulses then correspond to a serrated upper border of a rectangular area If the area enclosed by these lines, measured by means of a planimeter, is divided by the length of the horizontal base line (Fig 6, line L), the quotient represents the vertical distance above the zero line (Fig 6, line H) at which the mean arterial pressure lies By this method the mean arterial pressure is usually about one-third of the way between diastolic and systolic pressures, but varies with the configuration of the arterial pulse wave

Continuous Recording of Arterial Blood Pressure

Measurement of arterial blood pressures has long played an important role in cardiovascular research Recent developments in cardiac catheterization and the pulse-contour method of computing cardiac output have created widespread interest in accurately recording both pulmonary and systemic arterial pressures Pressure transducers suitable for recording the rapidly fluctuating arterial and intraventricular pressures, have certain essential requirements which should be understood by anyone who either uses them or wishes to appraise the multitude of clinical reports involving such equipment

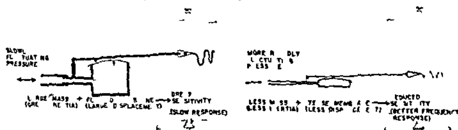
Rapidly fluctuating pressures can be accurately recorded only by apparatus with an

adequate frequency response The frequency response is a measure of the rate at which a recording system responds to a sudden change in pressure For example arterial pressure pulses cannot be accurately recorded by a mercury manometer because its inertia is very great in relation to the forces of displacement and restitution The factors which determine the responsiveness of a pressure-sensitive device can best be described in terms of simple mechanical systems

MECHANICAL PRESSURE TRANSDUCERS A common pressure transducer consists of a tambour with a rubber membrane coupled to a writing lever If the rubber membrane is quite flaccid very slight pressures will stretch the membrane and displace the writing lever (Fig 74) In response to an increased pressure a considerable quantity of fluid must pass along the tubing and enter the tambour to produce a corresponding displacement of the membrane and writing lever The inertia of the fluid and lever opposes a rapid response to a change in pressure, and the rubber membrane provides a relatively weak force to restore the fluid and lever to the initial position when the pressure is reduced Clearly, such a system could not respond rapidly enough to follow the fluctuating arterial pressure The natural frequency of a pressure transducer can be visualized in terms of a mass suspended on a spring The smaller the mass and the stiffer the spring the faster the oscillations which

MECHANICAL PRESSURE RECORDERS

A. MECHANICAL RECORDERS



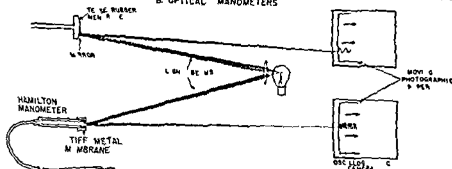


FIGURE A Pressure recording ordinarily involves the displacement of some type of elastic membrane To displace the membrane fluid must move into the recording capsule The inertia of the fluid the membrane and the recording mechanisms tends to resist displacement. When the moving mass is large and the membrane is flaccid, the recording system may be very sensitive to slowly fluctuating pressures but will not respond to rapid changes in pressure Reducing the moving mass and utilizing stiff membranes diminish sensitivity but improve the frequency response

B Optical manometers amplify the movements of stiff membranes by utilizing a weightless beam of light as a lever to produce rapid response with sufficient sensitivity For example the Hamilton manometer is equipped with a stiff beryllium-copper membrane which may respond reliably to frequencies in excess of 150 c.p.s

occur after a displacement from the rest position When the mass of the fluid and of the lever is large in relation to the tension of the membrane, *the oscillations are slow* If the rubber membrane is very tense, the frequency response is increased, but the sensitivity (deflection per unit of pressure) is correspondingly reduced (Fig 7*B*)

OPTICAL MANOMETERS By reducing the mass of the moving parts, greater sensitivity can be attained without sacrificing the frequency response The inertia of the writing lever can be eliminated by using a beam of light A small mirror eccentrically mounted on the membrane diverts a beam of light onto the slit of a recording camera (Fig 7*B*) Bulging of the membrane by increased pressure deflects the beam to a degree related to the magnitude of the applied pressure

Utilizing the increased sensitivity provided by a long weightless beam of light, Hamilton incorporated a beryllium-copper membrane with an eccentric mirror into a rigid system to produce a pressure recording device *with a frequency response ranging* above 150 cycles per second (Fig 7*B*) This manometer has been the accepted standard for the accurate recording of arterial blood pressure A more complete description of different mechanical pressure transducers was presented by Green[14]

ELECTRICAL PRESSURE TRANSDUCERS In this electronic age it is not surprising that slight movements of stiff membranes should be used to affect currents or voltages which can be amplified by vacuum tube amplifiers Various types of electronic pressure transducers are available in which movements of membranes produce changes in (*a*) resistance, (*b*) capacitance or (*c*) inductance (Fig 8*A*, *B*, *C*) In each case stiff membranes with small fluid displacement and relatively high frequency response can be used because the output signals can be amplified enough to activate recording galvanometers of various types

Resistance wire strain gauge manometers respond to a change in pressure with a change in the resistance to the flow of electrical currents when strain-sensitive wire is exposed to varying degrees of stretch A small bellows, used in place of a membrane, *is compressed* by increased pressure in the chamber (Fig 8*A*)

Variable capacitance manometers A stiff metal membrane separated from an electrode by a very *small air gap constitutes* a condenser (Fig 8*B*) Movements of the membrane in relation to the electrode vary the capacitance, which can be measured by means of a radio frequency circuit Such an instrument was described by Lilly in 1942,[15] and improved models of this manometer are now available commercially The membrane displacement of this device is extremely small (computed volume displacement, 0 00001 cc per 100 mm Hg) This characteristic permits successful recording of fluctuating pressures through long tubes of small caliber[16] The zero base line of this device tends to be more unstable than that of the unbonded resistance wire strain gauge

Variable inductance pressure gauges The *inductance of a coil can be altered* by changing the position of an iron slug within its magnetic field For example, if an iron slug connected to the center of an elastic membrane is mounted within two coils, deflection of the membrane moves the iron slug within the coils, changing their inductance Thus, changes in the inductance of the coils, recorded through an appropriate bridge circuit, indicate the amount the membrane is displaced during fluctuations in pressure Gauer and Gienapp[17] developed such an instrument which was so small it could be attached *to the end of a* cardiac catheter and introduced directly into the heart and great vessels A differential transformer pressure transducer was mounted within the thorax to record intraventricular pressures in dogs (see Chapter 6) Variable inductance gauges used to measure left ventricular diameter consisted of a single coil and a magnetic steel stylus (see Figs 6 7 Chapter 6)

AMPLIFICATION The output of unbonded strain gauge pressure transducers is suf-

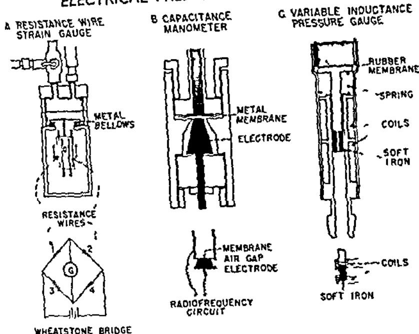


FIGURE 8 4 The unbonded resistance wire strain gauge (Statham gauge) consists of a metal bellows which is compressed by increased pressure within the chamber Downward displacement of the bellows is transmitted to a metal slide supported by four sets of strain-sensitive wires wound under tension and connected to form a Wheatstone bridge Displacement of the metal slide stretches two sets of wires and relaxes the other two These changes in resistance imbalance the bridge in proportion to the applied pressure The resulting voltage output from the bridge is amplified and recorded by various means

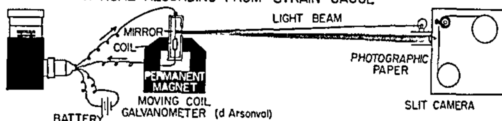
B The electrical capacitance diaphragm manometer is a condensor formed by an electrode (black) separated from a stiff metal membrane by a carefully adjusted air gap Displacement of the membrane changes the thickness of the air gap This results in a change in capacitance which is recorded by a radio frequency circuit. (From Lilly [15])

C Variations in magnetic flux in two coils of wire can be produced by movements of an iron slug positioned within the coils In a differential transformer pressure transducer the iron slug is fastened to the center of an elastic membrane so that changes in pressure produce changes in magnetic flux (From Gauer and Gienapp [17])

ficient to directly activate a sensitive moving-coil type of galvanometer (Fig 9 4) In this case the deflections are amplified by an optical system in which a light beam is deflected into an oscillograph camera This system is extremely stable and will retain the same sensitivity and zero base line for extended periods of time Such gauges can be obtained for a wide variety of pressure ranges so that either very large or very small pressure deviations can be recorded Once pressure recording is begun it is difficult to vary the sensitivity of the system However an amplifier can be used with optical galvanometers to adjust the sensitivity during recording To some investigators photographic recording is undesirable because the record cannot be observed as it is inscribed and processing the paper records is a nuisance

It is common practice to amplify electronically the signal emitted by the various pressure transducers to provide power sufficient to drive insensitive galvanometers In recent years direct writing recording instruments have become very widely used to record electrocardiograms and other physiologic phenomena The inertia of direct writing galvanometers is so great that their frequency response is limited and extensive amplification is required to produce any deflection at all Nevertheless it is possible to

AMPLIFICATION OF TRANSDUCER SIGNALS



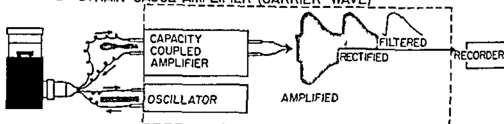


FIGURE 9 The weak signals from electronic pressure transducers generally require some form of amplification

A A Statham strain gauge powered by a constant voltage source and connected to a coil type galvanometer provides a very stable pressure recording system The deflections of the galvanometer can be amplified by an optical system deflecting a beam of light onto a strip of moving photographic paper

B Carrier wave amplifiers are frequently employed in conjunction with pressure transducers An oscillator supplies an alternating current of constant voltage to a Statham strain gauge Fluctuations in resistance in the bridge produce variations in the amplitude of this carrier wave The modulated carrier wave is then amplified and the resulting signal is then rectified filtered and recorded by suitable galvanometers

obtain accurate recordings of arterial and ventricular pressures under direct vision with such instruments (see Chapter 6) Many types of pressure transducer-amplifier combinations are available and a common type is illustrated schematically in Figure 9*B* A carrier wave type of strain gauge amplifier consists of an oscillator by which an alternating current of constant amplitude is *supplied to the Wheatstone bridge of the* strain gauge In passing through the bridge, the alternating current is modulated by the changing resistances in the bridge resulting from variations in pressure In other words, the amplitude *of the alternating current is* continuously affected by the varying resistances in the Wheatstone bridge which are, in turn, determined by the pressure applied to the bellows (Fig 9*B*) The output of the gauge enters a *capacity-coupled* amplifier which amplifies the modulated carrier wave Then the signals are rectified and the carrier wave is filtered out, leaving a D C voltage which powers a suitable recording device This general approach is widely used with many modifications to amplify the signals from different types of transducers

RECORDERS Three basic types of recording devices are employed to record pressure pulses (*a*) optical galvanometers, as in Figure 9*A*, (*b*) direct-writing galva nometers and (*c*) cathode ray oscilloscopes The *advantages and limitations of* optical galvanometers and direct-writing instru ments have been mentioned above Cathode ray oscilloscopes are well suited for the study of very rapidly fluctuating pressures, including heart sounds *In this instrument*, the amplified signals deflect an electron beam which has negligible inertia Such devices offer practically no frequency limitation The patterns are displayed on the face of the cath *ode ray tube and may be observed directly* or photographed

No ideal pressure recording system exists For any particular application the transducer, amplifier and recorder must be

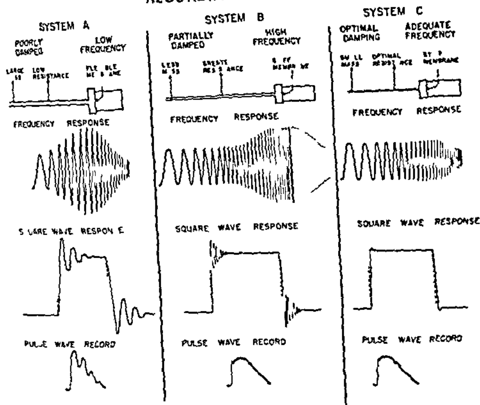


FIGURE 10 The response characteristics of a recording system should be carefully established and rechecked frequently

System *A* has a large *mass* of fluid in a large caliber tube and a flexible membrane Thus the system is very sensitive to changes *in pressure* but is poorly *damped*. *If* fluctuating pressures of constant amplitude and progressively increasing frequency are applied *to the* end of the tube the output from the system *increases* with higher frequencies up to the *natural* frequency of the system and then declines The characteristics of the system can be more easily checked by suddenly raising or *abruptly* lowering the pressure (a square wave *of* pressure) In this particular system, the *recorded* deflection was considerably delayed *in* reaching the new pressure level (slow *rise time*) The deflection had considerable overshoot and oscillations persisted at the natural frequency of the system for a considerable time (*poor damping*) This system would be entirely unreliable for recording arterial pressure pulses

System *B* has a stiff membrane and partial damping *Pressure* waves of equal amplitude produced a response of uniform height over a considerable range of frequency *However the deflections became exaggerated* near the natural frequency of the system. In response to a square wave the rise time was very short and the oscillations at the natural frequency of the system died down *rather promptly* This system would be adequate *for* recording *pressure* pulses unless certain portions of the pulse had *frequencies near the* natural frequency of the system. The square wave response should be determined *just before* using such a system because a single small air bubble in the catheter or the gauge may so reduce the *response* characteristics that *system B* acts like system *A*

In system C the membrane is more flexible than that in *system B* but system *C* has been critically damped. In other words *the output* from the system is uniform throughout a wide range of frequencies A square wave of pressure produced a rapid response and a very slight overshoot, but *no* sustained oscillations A critically damped system accurately reproduces arterial pressure pulses even though its uniform frequency response is limited to 20 or even 10 c p s (From records *presented by* Lambert, E. H. and Jones R E *Proc. Staff Meet. Mayo Clin.* 3 487–493 1948)

matched to obtain optimal performance This process invariably involves compromise of sensitivity, convenience, stability or frequency response The nature and significance of frequency response is widely misunderstood even by some individuals routinely engaged in physiologic recording

THE FREQUENCY RESPONSE OF RECORDING SYSTEMS It is generally agreed that high fidelity reproduction of a wave form can be recorded by a system which has a uniform response to the tenth harmonic of its fundamental frequency With a heart rate of 240 beats per minute, the pulse frequency is 4 per second and the tenth harmonic of this frequency is 40 c p s Such a high frequency response is deemed necessary if the most rapid changes in pressure during the pulse are to be faithfully recorded

Although it is possible to determine the frequency response characteristics of the transducer, amplifier and galvanometer individually, it is more important to test the dynamic response of the entire system assembled for use When the transducer is connected to a fluid-filled catheter or through tubing to a hypodermic needle, the frequency response of the gauge may be greatly reduced *The fluid in the system represents a* mass which must move with changes in pressure, and its inertia markedly reduces the frequency response of the gauge When the diaphragm is displaced by an increased pressure, its elasticity must overcome the inertia of the entire mass of fluid within the connecting tubes The mass of fluid can be reduced by using tubing of small caliber, but only at the price of increasing the frictional resistance to movement of fluid Thus, some of the pressure energy is dissipated as friction in fluid within narrow tubes Increasing the frictional resistance of a system is a form of "damping" By carefully matching the frequency response of the system with an optimal *degree of damping*, the response characteristics can be greatly improved (Fig 10) Damping is attained by reducing the caliber of the catheter or tube by locally constricting the tubing with a clamp or by inserting a short section of tube with appropriate caliber

Virtually identical arterial and ventricular pulse contours have been obtained with damped systems having uniform response to 5, 30 and 50 c p s [18] The frequency response and the degree of damping of any system should be routinely established by methods indicated in Figure 10 Such a procedure eliminates inaccurate records caused by temporary malfunction of the system For example, a small bubble remaining in the tubing or gauge after it is filled with fluid reduces the frequency response of the system to very low levels because air is much more elastic than the diaphragm

ARTIFACTS FROM THE MOVEMENT OF CARDIAC CATHETERS Pressures from within the heart and great vessels are frequently measured through long catheters Owing to movements of the heart, the tip of the catheter may oscillate in time with the cardiac cycle Such movements produce artifacts which are superimposed upon the pressure pulses and often attain amplitudes equivalent to 10 mm Hg These motion artifacts are much more prominent when recorded with high frequency systems and *are largely eliminated by using an* optimally damped system responding uniformly to 5 c p s [19]

SUMMARY

Stable or slowly fluctuating pressures can be accurately recorded with simple water or mercury manometers Arterial blood pressure can be measured indirectly by sphygmomanometry Accurate direct recording of rapidly fluctuating arterial or ventricular pressures can be accomplished *by means of* either mechanical manometers or electronic transducers of various types It is vitally important to test the frequency response and degree of damping of any system which is employed for accurate registration of rapidly fluctuating pressures

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Chapter 11

The Size and Configuration of the Heart

Most forms of organic heart disease produce a chronic load on the heart If the stress is of sufficient intensity and duration, the heart enlarges during the course of the disease Detecting enlargement of a specific portion of the heart would be very simple indeed if the size, configuration and orientation of the heart were constant in all normal individuals However, there are many sources of variation in these factors Massive enlargement of cardiac chambers can usually be recognized easily but a diagnosis at this stage *is of limited value to the patient since* opportunities for preventive therapy have been lost During the early stages of heart *disease when accurate diagnosis has maximum* value, the size and configuration of the heart generally remain within the "normal range" Small degrees of enlargement can be discovered only by considering whether the size and shape of the heart are normal for the particular patient Such a judgment requires constant awareness of the sources of variation in cardiac size and configuration, supplemented by experience in evaluating the "normal range" encountered in patients of different habitus, age and sex This decision must also be based on supplemental information derived from the clinical history, physical examination and laboratory tests Since an incorrect diagnosis of heart disease may produce invalidism or cardiac neurosis, *recognizing normality and detecting abnormality* have equal importance Therefore, the limitations of any diagnostic method must be *fully understood*

ORIENTATION OF THE HEART WITHIN THE THORAX

A major source of variation in apparent heart size is the fact that the heart occupies an asymmetrical position within the thorax The septa which divide the atria and ventricles are oriented between the sagittal and frontal planes of the thorax A frontal view of the heart (Fig 1*A*) discloses the right atrium, right ventricle, pulmonary conus and aortic arch with a small portion of the left ventricle appearing on the left border On the posterior aspect of the heart lie the remainder of the left ventricle, the left atrium and a portion of the right atrium A transverse section through the thorax (Fig 1*B*) *indicates the relation of the heart and the* thoracic walls The cardiac chambers are separated from the anterior and lateral *thoracic walls by varying amounts of lung* tissue except near the apex of the heart Here the right ventricle near the interventricular groove makes contact with the precordium

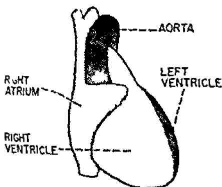
THE POINT OF MAXIMAL IMPULSE

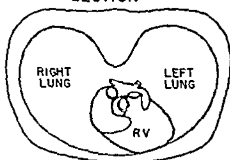
During early systole in most individuals, a circumscribed thrust appears in the *fifth* intercostal space near the *left mid-clavicular* line (Fig 2) The origin of this impulse has long been attributed to the impact of the ventricles as the heart rotates during contraction A more reasonable explanation was proposed in 1891 by Haycraft,[1] who observed that the flaccid ventricular chambers are easily deformed during diastole At the beginning of systole, the contracting ventricular walls suddenly assume a more rounded contour and recoil away from the area of compression The free wall of the right ventricle near the apex of the heart is in contact with the anterior chest wall (Fig 1*B*) This portion of the ventricle is flattened during diastole and abruptly assumes a convex contour during the subsequent ventricu-

lar contraction This action causes forward displacement of intercostal tissues near the apex of the heart—the so-called apical thrust Burchell and Visscher demonstrated by high-speed motion pictures that the inflow tract of the right ventricle contracts before the outflow tract so that blood is first shifted from the inflow tract into the outflow channel and then ejected into the pulmonary artery

It is generally stated that the point of maximum impulse is approximately 1 cm to the right of the cardiac apex However, it is clear that the distance between the point of maximal impulse and the apex of the heart must depend upon the site of contact between the anterior surface of the heart and the anterior thoracic wall (see Fig 1B) Thus, the configuration of the heart and anterior thoracic wall must have an important bear-

THE ORIENTATION OF THE HEART WITHIN THE THORAX





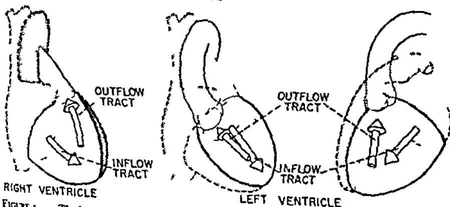


FIGURE 1 The heart is asymmetrically oriented within the thorax.

A In the frontal view the right atrium is situated on the right side with the right ventricle on the anterior surface A small portion of the left ventricle appears on the left border The superior vena cava aorta and pulmonary artery a e grouped above tl e heart in the upper mediastinum

B Viewed from above the heart occupies an oblique position within the thorax with the right ventricle making contact with the anterior thoracic wall to the left of the midline

C Blood entering the ventricular chambers tends to flow from the atrioventricular valves toward the apex of the heart. This inflow tract in each ventricle is indicated by an arrow drawn from the center of the A V val es to the apex The outflow tract is described by an arrow extending from the apex of the ventricle to the center of the corresponding semilunar valve In the right ventricle the inflow tract makes an angle of more than 45 degrees with the outflow tract. In contrast, the left ventricular inflow and outflow tracts are almost parallel owing to the cylindrical shape of the chamber

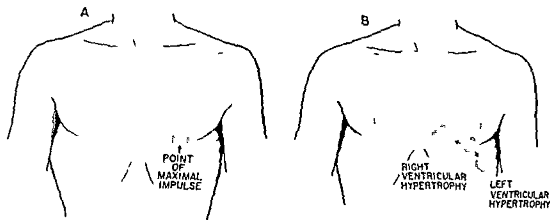


FIGURE 2 *A* During each cardiac contraction, a thrust can be observed and palpated in a small area on the precordium located in the fifth intercostal space medial to the mid-clavicular line in the average normal individual

B The point of maximal impulse is displaced downward and to the left by elongation of the left ventricle The right ventricle enlarges anteriorly toward the sternum and produces a diffuse impulse over a considerable area between the mid-clavicular line and the sternum (see Fig 1*B*)

ing on the position of the cardiac impulse The point of maximal impulse may be *imperceptible in patients with emphysema or* very thick chest walls

It is frequently stated that whenever the point of maximal impulse lies to the left of the mid-clavicular line or more than 10 cm to the left of the midline, the heart is probably enlarged Actually, this is a sign of left ventricular enlargement However the point of maximal impulse does not bear a constant relation to the apex of the heart, so no rule of thumb can be safely used to describe the limits of normal The location of the point of maximum impulse must be interpreted in terms of the individual s habitus as well as of other causes of variation in the orientation and size of the heart These will be discussed in a subsequent section (see *Roentgenographic Examination of the Heart*) Massive ventricular enlargement may displace the apical impulse enough to provide a definite indication of abnormality For example, a point of maximal impulse located at the left anterior axillary line or in the axilla is a reliable sign of left ventricular enlargement Under these circumstances there should be other obvious signs of advanced heart disease Lesser degrees of ventricular enlargement may be missed or overemphasized, and should be confirmed by roentgenographic examination When the right ventricle becomes enlarged *it tends to protrude anteriorly toward the* sternum Under these conditions a diffuse precordial impulse may be palpated over a fairly wide area to the left of the sternal margin Progressive enlargement of the right ventricle in young children often produces a protuberance of the left precordium

PERCUSSION OF THE HEART

The technique of percussion was originated by Leopold Auenbrugger (1761) as a result of the observation that the quantity of wine in a barrel can be estimated by tapping the end and noting the resonance [3] When a sharp tap is delivered to the thoracic wall, the underlying tissues are suddenly displaced Due to their elasticity, they rebound and oscillate while the imparted energy is dissipated The ensuing vibrations have four characteristics important in percussion (1) frequency (2) quality (3) duration and (4) intensity (see Chapter 13) The frequency of vibration depends upon the elasticity of the structures in relation to the mass of tissue in vibration (see Chapters 10 and 13) which in this case includes tissues of varying density and elasticity (e g , muscle, fat bone, lung)

The vibrations produced by percussion over a well inflated lung appear to have relatively high intensity (loudness) low frequency (pitch) and long duration (resonance) A region of absolute dullness may be outlined over the precordium (Fig 3) The

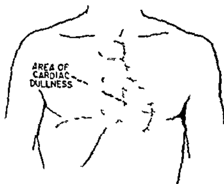


FIGURE 3 The size of the heart can be approximated by skilled percussion over the precordium. The region of dullness to percussion is always smaller than the actual size of the heart because of its rounded contour (see Fig 1B) Severe cardiac enlargement consistently produces expansion of the area of dullness but minor degrees of enlargement cannot be reliably detected

percussion note over this area has relatively low intensity high pitch and short duration (reduced resonance) Extending beyond the region of absolute dullness is an area of relative dullness which approximately delineates the heart borders (Fig 3) The area of relative dullness is not sharply defined The rounded surfaces of the heart do not conform to the anterior thoracic wall (see Fig 1B) and the heart borders outlined by percussion tend to be smaller than the silhouette observed on roentgenograms by 1 0 to 1 5 cm or more

Percussion combined with palpation of the point of maximal impulse has value as an adjunct in arriving at a clinical impression They are not suitable for detecting *early* cardiac enlargement because their inaccuracy is superimposed upon the normal variability in cardiac size and configuration which will be discussed below Advanced enlargement of the left ventricle can often be detected with confidence However, a patient with other signs of heart disease should not be denied roentgenographic examination just because the heart size appears normal from percussion of the precordium or palpation of the precordial impulse

ROENTGENOGRAPHIC EXAMINATION OF THE HEART

When x rays penetrate the chest absorption of the radiation depends upon the effective *radiodensity of the tissues lying in the* path of each ray The heart has greater radiodensity than the aerated lung Roentgen rays which are not absorbed during penetration of the tissues can be used to illuminate a fluorescent screen (fluoroscopy) or to expose a photographic plate clamped between fluorescent intensifying screens in a cassette (Fig 4) X ray films are routinely exposed with the tube at a distance of 2 m from the film cassette and are identified as teleroentgenograms (*tele* = distance) The image of the cardiac silhouette on a fluorescent screen may be recorded by motion picture photography or cinefluorography [4,6] Regardless of the technique, roentgenography serves to reveal the size and configuration of the cardiac silhouette as projected on a single plane

The Cardinal Positions for Cardiac Roentgenography

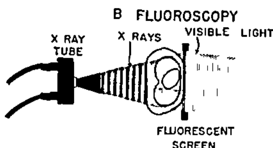
As the heart appears in silhouette on either roentgenographic plates or fluoroscopic screens only those portions of the heart which appear on the borders can be observed Obviously not all the chambers can appear on the borders in any one view For this reason a complete roentgenographic examination of the heart requires studying the cardiac silhouette from several views Three standard positions are commonly used by cardiologists—the postero-anterior the left anterior oblique and the right anterior oblique positions In each case the cassette or fluorescent screen is perpendicular to the central ray emitted by the tube In the

METHODS OF ROENTGENOGRAPHY

A TELEROENTGENOGRAPHY



B FLUOROSCOPY



C CINEFLUOROGRAPHY



FIGURE 4 As x rays penetrate the body the tissues absorb the rays in relation to their radiodensity The rays which penetrate the body delineate the borders of internal organs on either x ray films or the surface of a fluorescent screen

A Teleroentgenograms are x ray plates exposed with the tube 6 ft or 2 m from the x ray film. At this distance the distortion of the heart size by the diverging rays is not misleading

B Fluoroscopy is accomplished by observing directly the visible light emitted by fluorescent screens exposed to x rays The tube is fairly close to the screen and the image of the heart is enlarged about 15 to 20 per cent by the diverging rays

C Cinefluorography involves motion picture photography of the images on fluorescent screens Examples of cinefluorographic recordings have been presented in Chapter 1 (see Figs 9 and 13)

postero-anterior position, the patient stands squarely before the screen or cassette with the front of his chest pressed evenly and firmly against it (Figs 5*B*, 6*B*) This is the most common position for cardiac and pulmonary roentgenography The left anterior oblique view is attained by rotating the patient approximately 50 degrees so that his left shoulder is toward the screen or cassette (Figs 5*A*, 6*A*) A patient facing the screen is rotated 45 degrees so that his right shoulder is toward the screen to view the heart in the *right anterior oblique position* (Figs 5*C*, 6*C*) Rotating the patient 90 degrees from the postero-anterior position presents the lateral view, which is frequently employed by roentgenologists but not as commonly used by cardiologists

THE POSTERO-ANTERIOR POSITION When the heart is viewed in the postero-anterior position (Figs 5*B*, 6*B*), the rounded outline of the right atrium appears in the lower half of the right border of the heart The junction between the right atrium and the superior vena cava is indicated by an obtuse angulation Slight rotation of the patient to the right may expose the first portion of the ascending aorta just above the right atrial border The upper half of the right border of the heart generally corresponds to the border of the superior vena cava and the brachiocephalic vessels The ascending aorta, passing obliquely upward and to the right across the upper mediastinum is not visible in the postero-anterior position The uppermost *portion of the aortic arch* appears as a knob on the left border of the cardiac silhouette just below the level of the sternoclavicular junction Below the aortic knob and extending to approximately the mid point of the left border of the heart is the pulmonary artery Along the lower half of the left border is the shadow of that portion of the left ventricle near the interventricular groove There is usually a slight angulation at the junction between the pulmonary

THREE STANDARD POSITIONS FOR CARDIAC ROENTGENOGRAPHY

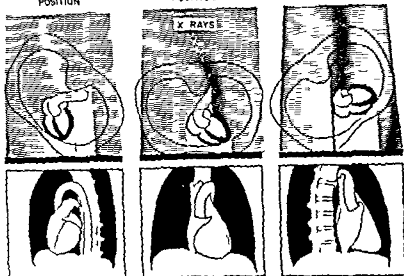


FIGURE 5 A complete roentgenographic examination of the heart requires study of the cardiac silhouette in three positions The orientation of the heart in each position is indicated schematically in a transverse section and on a teleroentgenogram. For labels see Figure 6.

A To assume the left anterior oblique position, the patient turns with his left shoulder toward the x-ray cassette until the sagittal plane of his body makes an angle of 50 degrees.

B In the postero-anterior position, the sagittal plane of the body is parallel with the cassette, which is in firm contact with the anterior thoracic wall.

C In the right anterior oblique position, the patient rotates his right shoulder toward the cassette or screen until the sagittal plane of the body makes an angle of 45 degrees

THE CARDIAC SILHOUETTE IN THREE STANDARD POSITIONS

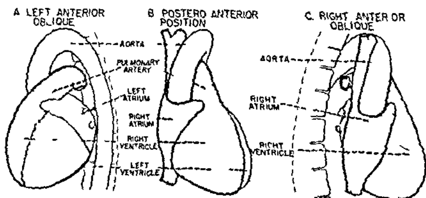


FIGURE 6 *A* The left anterior oblique position is best suited to determine the extent to which either the right or the left ventricle is enlarged, since they appear on opposite borders of the cardiac silhouette The aortic arch is also best observed in this view

B In the postero-anterior position neither the right ventricle nor the left atrium is represented on the borders of the cardiac silhouette However enlargement of the left ventricle and right atrium is best seen in this view

C The right anterior oblique position provides the best view for demonstrating dilatation of the left atrium

artery and the left ventricular shadow, which *is called* the cardiovascular angle During *systole, the segments* above and below the cardiovascular angle tend to move in opposite directions because the pulmonary artery is distended as the ventricles contract The point of opposite pulsation at the apex of the cardiovascular angle is an important landmark *during fluoroscopy* (see Fig 8) In *some cases the tip of the left* auricle appears *at the cardiovascular* angle, but its position *or movement* is not apparent

THE LEFT ANTERIOR OBLIQUE POSITION When a patient is rotated to the left anterior oblique position (Figs 5*A*, 6*A*), the right and *left* ventricles are on opposite sides of the silhouette and their relative sizes can be appraised An angulation of the silhouette near the mid-point of the sternal margin of the heart represents the juncture of the right ventricular outflow tract with the root of the ascending aorta The entire arch of the aorta is sometimes visible in this view although it may be obscured by the dense overlying structures such as the scapula and vertebral *spine The left* atrium occupies a position *between the base of the left* ventricle and the bifurcation of the pulmonary artery This portion of the border is also partially obscured by superimposed structures

THE RIGHT ANTERIOR OBLIQUE POSITION In the right anterior oblique position, the outflow tract of the right ventricle appears on the sternal border of the heart The ascending aorta appears in profile in the superior half of the cardiac shadow The left atrium occupies a position near the center of the vertebral aspect of the cardiac silhouette with the right atrial border just below If the patient is properly oriented, a region of low density appears between the posterior aspect of the heart and the vertebral spine the retrocardiac space The esophagus passes down the posterior mediastinum and is in apposition with the left atrium along its course The esophagus filled with a radiopaque mixture of barium outlines the left atrial border and its motion can be clearly observed fluoroscopically The right anterior oblique view is particularly useful for detecting early dilatation of the left atrium (see Fig 12)

SOURCES OF VARIATION IN THE CARDIAC SILHOUETTE

Roentgenographic *interpretation is complicated by* a number of *factors which are not* necessarily related to cardiac size or function Certain of these conditions cause the normal heart to appear large Others tend to cause an enlarged heart to appear normal in size For this reason it is convenient to speak of the "apparent" size when considering the sources of variation in the cardiac silhouette The sources of variation in the cardiac silhouette can be divided into two main categories (*a*) individual variation and (*b*) technical variation By careful standardization of the roentgenographic technique, technical variation can be largely eliminated Individual variation must be recognized by the physician and evaluated in each individual case

Individual Variation

The most important initial step in the roentgenographic examination of a patient is to visualize the "normal" range of size and configuration of the heart for a person with his particular habitus and extracardiac conditions Proficiency in this essential feature of the examination is gained only through experience Sound judgment can be developed simply by taking advantage of every opportunity to correlate the roentgenographic appearance of the heart with the habitus and cardiac condition of patients

HABITUS In asthenic individuals, the thoracic cavity is long and narrow so that the long axis of the ventricles approaches a vertical orientation (Fig 7) The cardiac silhouette is narrow and the left border may lie several centimeters inside the mid-clavicular line Enlargement of the heart tends to restore the apparent cardiac size toward the normal configuration In patients of this sort, a considerable degree of left ventricular enlargement is required to bring the left border of the heart to the mid-clavicular line,

which is within the normal range for the average individual For this reason early ventricular enlargement is frequently overlooked in patients in whom the resting position of the diaphragm is lower than average

In contrast a patient with a stocky build characteristically has an elevated diaphragm (Fig 7) When the longitudinal axis of the

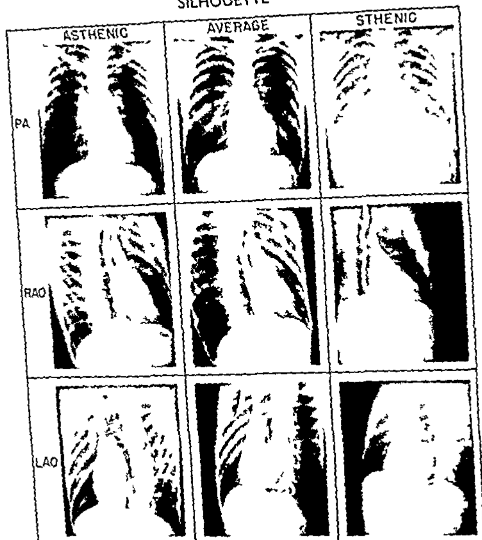


FIGURE 7 Roentgenograms obtained on three normal individuals of different habitus in the three cardinal positions indicate the variation in the shape and apparent size of the normal cardiac silhouette

In asthenic individuals the thorax is long and narrow so the heart assumes a vertical position The cardiac silhouette is so narrow that severe enlargement of the heart may be overlooked in such patients

If all patients had average habitus criteria for enlargement of the individual chambers could be easily established and slight changes could be consistently detected

In sthenic individuals the high diaphragm supports the heart in a horizontal position The wide cardiac silhouette gives the impression of left ventricular enlargement and accentuation of the pulmonary vascular markings suggests pulmonary congestion These factors must be constantly evaluated in analyzing roentgenographic images

Note that the right dome of the diaphragm in the three individuals is at the level of the eleventh, tenth and eighth costovertebral junctions respectively

heart approaches a horizontal position, even a heart of normal size may appear enlarged In such a patient the pulmonary markings are accentuated, the cardiovascular angle is more acute, and the apex of the heart is displaced toward the left In short, such a normal individual could easily be mistaken for a patient with serious left ventricular enlargement and pulmonary congestion Thus, an important step in roentgenographic interpretation is determining the habitus of the patient and the relative height of the diaphragm For this purpose, it is convenient to establish the level of the dome of the diaphragm in relation to the costovertebral junctions (Fig 7)

VARIATION IN PATIENTS WITH THE SAME HABITUS Individual variation is a constant problem in anatomy, physiology and clinical medicine The cardiac silhouettes of different patients of similar age, sex, habitus and physical condition may vary rather strikingly These changes may be explained in terms of the orientation of the heart within the thorax or of developmental variations of the heart, lungs or thoracic cage Obviously, individuals in different age groups with the same type of habitus may have significantly different cardiac silhouettes Again, wide experience is the most important factor in this type of evaluation

THE PHASE OF THE CARDIAC CYCLE Teleroentgenograms are generally exposed during a very brief period of time (e g , one-fifth to one-sixtieth of a second) Since the diastolic interval is somewhat longer than the duration of systole, more than half of a series of teleroentgenograms will be exposed during diastole However, more than one-third of the teleroentgenograms are exposed during some phase of systole Fortunately, the change in the size and shape of the cardiac silhouette during the cardiac cycle is rarely sufficient to produce any serious error from this source (see Fig 8)

THE PERICARDIAL FAT PAD In many normal individuals, a triangular shadow appears at the apex of the heart which is due to the accumulation of fat in this region Elongation of the left ventricular outflow tract and displacement of the apex downward and to the left might be erroneously suspected unless the region is carefully scrutinized It is generally possible to detect the apical border passing through the shadow of the pericardial fat pad

DISPLACEMENT OF THE HEART The heart does not always occupy its normal position within the thorax For example, the heart may be displaced toward the left either by atelectasis in the left lung or pressure pneumothorax in the right pleural cavity In either case, the left border of the heart moves toward the left and the right border may overlie the spine If the pulmonary condition is unrecognized, the patient may be incorrectly suspected of having cardiac enlargement

DEFORMITIES OF THE THORAX If the lower end of the sternum is depressed (funnel chest) the distance between the sternum and the vertebral spine is reduced The heart may be compressed in its postero-anterior dimension and displaced toward the left The left border of the heart may become rounded, giving the impression of ventricular enlargement

In kyphoscoliosis, the abnormal curvature of the vertebral spine may produce cardiac displacement as well as a change in the "apparent" cardiac configuration The border of the curved vertebral spine may be confused with the cardiac silhouette, giving an impression of cardiac enlargement

Technical Variation

The technique of roentgenography must be carefully standardized to consistently produce films which can be reliably interpreted The apparent size and shape of the heart may be seriously distorted by thoughtless or careless technicians

INACCURATE POSITIONING OF THE PATIENTS If the patient is correctly placed in the postero-anterior position, the manubrium of the sternum should be centered over the vertebral bodies If the patient is rotated even slightly from this position, the apparent

configuration of the heart may be significantly altered (Figs 6, 7) Similarly the configuration of the heart and its position in relation to the thoracic spine are seriously distorted by either inadequate or excessive rotation of the patient to obtain oblique views of the heart Standardization of patient positioning is essential for accurate evaluation of teleroentgenograms This problem need not arise during fluoroscopy because the examiner can view the heart from all angles and control the positioning during visualization.

Respiratory Activity The level of the diaphragm is influenced by the phase of respiration in which the teleroentgenogram is exposed If the x ray technician instructs the patient to take a deep breath prior to exposing the x ray plate the level of the diaphragm is depressed and the longitudinal axis of the heart assumes a more nearly vertical position (Fig 8) On the other hand the patient may be instructed to press against the x ray cassette, in which case he may forceably exhale elevating the level of the diaphragm Changes in the level of the diaphragm due to respiratory activity may seriously distort the apparent cardiac size (Fig 8)

The Valsalva Maneuver A patient instructed to hold his breath may inadvertently or unconsciously raise the pressure within the thorax—the Valsalva maneuver The increased intrathoracic pressure impedes the blood flow into the thorax and causes a progressive reduction in the size of the heart. Under these conditions the actual size of the cardiac silhouette may be significantly reduced 7 The sources of variation due to respiratory activity and the Valsalva maneuver can be largely eliminated by well trained technicians

THE RELATIVE ADVANTAGES OF ROENTGENOGRAPHIC TECHNIQUES

All of the sources of technical variations listed above apply to teleroentgenography and may be avoided during fluoroscopy Furthermore, the roentgenograms are frequently interpreted without any information concerning the patient—a serious limitation indeed In the course of fluoroscopy, the examiner has an opportunity to note the habitus of the individual and the presence of thoracic and spinal deformities He is in a position to check his observations by inquiring into the clinical history and to perform a physical examination when indicated He can observe the changes in size configuration

THE EFFECTS OF RESPIRATION ON THE CARDIAC SILHOUETTE

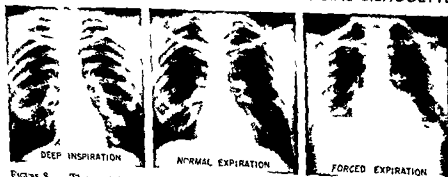


Figure 8 Three roentgenograms from a single normal subject illustrate the changes in shape and apparent size of the cardiac silhouette which can be produced by deep inspiration and forced expiration. In the center the changes in the cardiac silhouette during a cardiac cycle are indicated by dotted lines based on cinefluorographic studies of normal human hearts. The arrow indicates the cardiovascular angle at the junction of the left ventricle and the pulmonary artery on the left border During systole the left ventricular margin moves in while the pulmonary artery expands. Since the upper and lower limbs of the cardiovascular angle move in opposite directions, the apex of this angle is often called the point of opposite pulsation, a prominent landmark during fluoroscopic examination.

and position of the heart and great vessels during the cardiac cycle and view the heart from all aspects

Fluoroscopy has practical limitations Because of radiation hazards, the illumination of the fluorescent screen is maintained at an absolute minimum consistent with the adequate visualization of the image after at least 15 to 20 minutes of dark adaptation Brightness and contrast of the images are barely adequate, the excellent definition of cone vision is sacrificed and the comparatively coarse rod vision must be used For these reasons, much of the detail on the fluoroscopic image cannot be seen under routine conditions The total duration of radiation exposure must be held at a minimum (e g , 30 to 60 seconds if possible) This can be accomplished by relatively brief examination of the cardiac silhouette and by turning the machine off while the patient is positioned The volume of tissue irradiated should be minimized by reducing the field of examination to include only the areas under scrutiny Maximum information with minimal radiation can be attained only by training and experience Fluoroscopy of patients should be undertaken only with complete understanding of the hazards of radiation and methods of minimizing the risks to both the patient and the examiner The advent of screen-intensifying techniques promises to alleviate these difficulties in laboratories equipped with this apparatus

The only permanent record obtained from routine fluoroscopy is a written description of the observations Detection of changes during serial examinations is very difficult since a description of the cardiac silhouette in the various positions does not convey a complete or accurate impression of the image

In spite of their limitations teleroentgenographic films constitute a permanent record of the size and shape of the cardiac silhouette at the instant of the exposure Films taken years apart may be compared for indications of change in contour or in chamber size Teleroentgenograms may be viewed as long as desired under adequate illumination The light intensity and the contrast between light and dark shadows greatly exceed those available during fluoroscopy The quantity of radiation for a single x-ray exposure is significant, but not excessive However, serial teleroentgenograms should not be ordered freely without considering the total radiation being administered to the patient

Cinefluorography combines the advantages of fluoroscopy and teleroentgenography [8, 11] During projection, the films reveal the fluoroscopic images in motion with ample light intensity and good contrast The principal disadvantages at present are that (1) the duration of the exposure is only about 10 seconds with radiation roughly equivalent to fluoroscopy for 1 minute, (2) it is difficult to obtain films in the three fundamental positions within 10 seconds' exposure time and (3) the films are more difficult to process and file The first two disadvantages are greatly alleviated by fluoroscopic screen intensification [12]

MEASUREMENTS OF THE CARDIAC SILHOUETTE

Detection of cardiac enlargement is generally a more or less subjective judgment in view of the numerous causes of variation described above A more scientific approach to roentgenographic interpretation has been attempted by measuring various dimensions of the cardiac silhouette Information concerning the length or width of the individual ventricular chambers would be most helpful However the position occupied by the atrioventricular valve rings cannot be accurately identified, with the result that most of the measurements include both atrial and ventricular dimensions Further, the dense shadows cast by abdominal organs largely obscure the inferior margin of the cardiac silhouette The transverse diameter is the most common measurement in current use To determine this dimension, a vertical line is inscribed over the vertebral spine on a teleroentgenogram exposed in the postero-

anterior position The point on the right border of the heart which is farthest from the midline is selected by inspection (in the midportion of the right atrial border) From this point a line is drawn perpendicular to the vertical reference line In the same way a perpendicular is erected from the point on the left border of the heart which is most distant from the midline The sum of the two horizontal segments is called the transverse diameter (Fig 9)

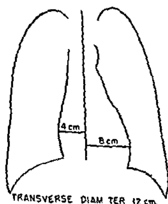
In view of the extreme variation in different individuals this measurement has no significance without reference to the habitus of the individual (Fig 7) A fairly common practice is to divide the transverse diameter of the heart by the width of the thorax (the cardiothoracic ratio) It is frequently stated that a cardiothoracic ratio of more than 0 5 indicates cardiac enlargement This assumption may have some validity among individuals of average body build However a vertically placed heart may be considerably enlarged before reaching a cardiothoracic ratio of 0 5 If the long axis of the heart approaches the horizontal, the cardiothoracic ratio may exceed 0 5 without any cardiac enlargement The cardiothoracic ratio has little value and may be seriously misleading

To overcome this deficiency Ungerleider et al [13,14] measured the transverse diameter of a large group of normal individuals and devised tables by which it is possible to predict the transverse diameter of an individual according to his weight height age and sex If the measured transverse diameter of a patient exceeds the predicted dimension by more than 10 per cent he probably has an enlarged heart

Before using the transverse diameter as a criterion of cardiac enlargement the following limitations must be recognized (*a*) the measurement includes both the right atrium and the left ventricle, (*b*) the ventricular chambers do not enlarge *primarily* along a horizontal axis (*c*) elongation of the outflow tract of the left ventricle would be detected but there is no representation by the right ventricle *in this measurement* and (*d*) the application of the measurement presupposes

CARDIAC MEASUREMENTS

A. TRANSVERSE DIAMETER



B CARDIOTHORACIC RATIO

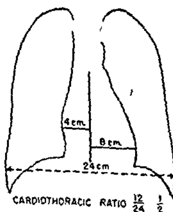


FIGURE 9 *A* The transverse diameter of the cardiac silhouette is measured from a vertical line along the vertebral spine. The maximum distances from this line to the right and left borders of the heart shadow are added to measure this dimension Although neither of these points of measurement is particularly appropriate for detecting chamber enlargement, no other dimension has proved more revealing

B The quotient obtained when the transverse diameter is divided by the width of the thoracic cage at its widest point is termed the cardiothoracic ratio This device is intended to correct for differences in habitus among patients If the ratio exceeds 0 5 cardiac enlargement is said to be present. The extent to which this measurement can be misleading is indicated by a glance at Figures 7 and 8

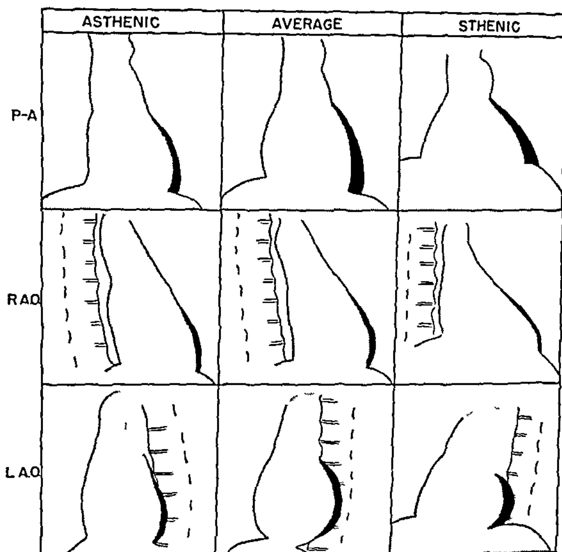


FIGURE 10 The most common type of left ventricular enlargement is an elongation of the chamber which displaces the apex downward and to the left This change is most easily observed in the postero-anterior projection but is often difficult to detect in asthenic patients and may be exaggerated in sthenic patients In the left anterior oblique position an enlarged left ventricle extends posteriorly beyond the vertebral spine to an abnormal degree Severe left ventricular enlargement may produce a bulge on the lower portion of the sternal margin of the silhouette in the right anterior oblique position

that the sources of variation other than habitus, age and sex have been eliminated or controlled It is more important to determine which chamber is involved than to establish that the heart is enlarged If these restrictions are recognized, the tables of *Ungerleider and Clark may serve a useful* purpose

ENLARGEMENT OF THE CARDIAC CHAMBERS

It is impossible to illustrate here the characteristic changes in the heart shadow produced by individual chamber enlargement under all possible circumstances Teleroentgenograms in the postero-anterior and right and left anterior oblique positions from three normal individuals with different habitus have been chosen The effects of *enlargement of each cardiac chamber* are illustrated on these "normal" silhouettes This method of representation illustrates the effects of varying habitus on roentgenographic interpretation, but it must be emphasized that orientation of the heart is only one of many sources of variation

Left Ventricular Enlargement

The principal sign of left ventricular dilatation is elongation of the outflow tract, which is most clearly visualized in the postero-anterior position (Fig 10) The longitudinal axis of the heart tends to elongate, displacing the apex downward and to the left Since the diaphragm limits the amount of the caudal expansion the longitudinal axis of the heart tends to rotate toward the horizontal The great vessels retain their normal position For this reason the cardiovascular angle becomes more acute (see Fig 8) As the left ventricle elongates the apex of the cardiovascular angle (point of opposite pulsation) is generally located above the mid point on the left border of the silhouette The ventricles may also rotate around the longitudinal axis of the heart, but this has little effect on the cardiac configuration

In patients with asthenic habitus and vertically oriented hearts, rather severe degrees of left ventricular enlargement must develop before these changes are beyond the range observed among normal individuals with average body build

Since the left ventricle appears enlarged

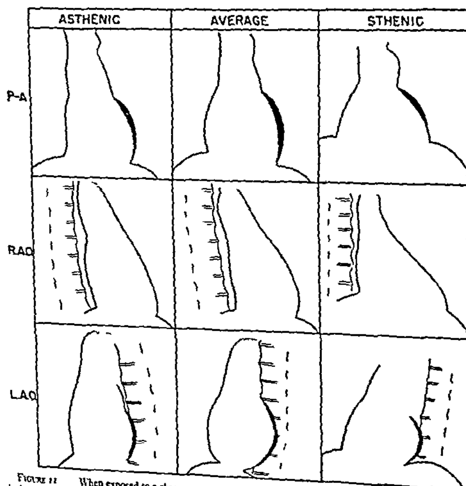


FIGURE 11 When exposed to a chronic pressure load the left ventricle may become more spherical with little or no enlargement of the heart shadow This *concentric hypertrophy* produces a rounding of the cardiac silhouette in the frontal view However this change is frequently no greater than that encountered among normal individuals and is difficult to demonstrate with confidence

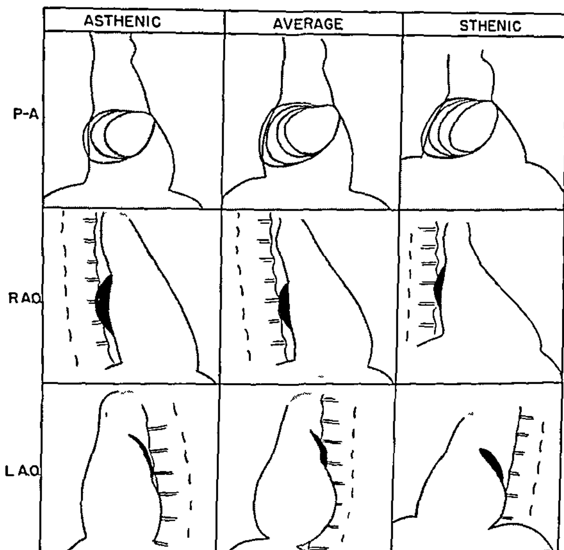


FIGURE 12 The left atrium is situated on the posterior aspect of the heart Dilatation of this chamber produces displacement toward the right around the back of the heart For this reason rather extreme left atrial enlargement may be completely invisible in the postero-anterior projection On the other hand the first sign of left atrial dilatation can be observed in the left anterior oblique view where the expanding chamber encroaches upon the retrocardiac space In the left anterior oblique position extreme left atrial enlargement may be observed particularly if it produces upward displacement of the left main bronchus

in the normal sthenic individual even slight degrees of further elongation may displace the apex well beyond the mid-clavicular line The normally prominent cardiovascular angle generally becomes accentuated

In the left anterior oblique position, the posterior margin of the cardiac silhouette is displaced backward and overrides the spine to a greater extent than normal During fluoroscopy, the patient is frequently rotated until the left ventricular border clears the spinal shadow According to Wilson et al [15] the amount of rotation required may be expressed in degrees (the angle of clearance) as an indication of left ventricular enlargement

CONCENTRIC HYPERTROPHY OF THE LEFT VENTRICLE An increased pressure load on the left ventricle results from aortic valvular stenosis or systemic arterial hypertension Judging from the cardiac size of patients with essential hypertension [16] the response of the left ventricle is extremely variable In some cases, marked cardiac enlargement was present for 10 years or more with little functional limitation In others the heart remained

normal in size in the presence of congestive heart failure In some patients with hypertension hypertrophy of the ventricular wall may completely compensate for the load without cardiac dilatation Under these circumstances the ventricular border of the heart becomes rounded a condition called concentric hypertrophy (Fig 11) Superficially the ventricle appears to have assumed a more spherical shape as viewed in the postero-anterior position The cardiovascular angle is more acute but the apex of the heart is not displaced downward or to the left Concentric hypertrophy has little effect on the cardiac silhouette in the oblique views

Left Atrial Dilatation

No portion of the main left atrial chamber appears on the border of the cardiac silhouette in the postero-anterior position Enlargement of the left atrium extends posteriorly and toward the right, as indicated by the dotted lines in Figure 12 Massive dilatation of the left atrium may extend so far toward the right that a double shadow is observed along the right border This double

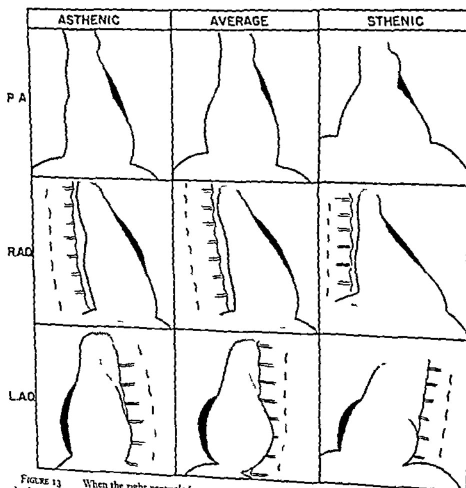


FIGURE 13 When the right ventricle becomes enlarged the outflow tract and the pulmonary artery are displaced upward and to the left so that the cardiovascular angle becomes straightened or convex. This is the only sign which can be observed in the postero-anterior view The anterior protrusion of the chamber is best observed in the left anterior oblique position, and to a lesser extent in the right anterior oblique view Right ventricular enlargement is most commonly encountered in children with congenital heart disease or rheumatic mitral valvular disease.

shadow is composed of the right atrial margin superimposed upon the dilated left atrial chamber

Early dilatation of the left atrium may be detected in the right anterior oblique position Displacement of the dilated left atrial wall encroaches upon the retrocardiac space in the midportion of the cardiac silhouette The barium-filled esophagus may be displaced posteriorly and toward the right by the distending atrial chamber In early mitral stenosis, left atrial dilatation of this type may be the only objective evidence of organic heart disease

In the left anterior oblique position, the left atrium is frequently difficult to visualize *Enlargement of the left atrium is not observed in this view at an early stage* Massive left atrial enlargement may elevate and compress the left main bronchus, producing a dry, hacking cough

Right Ventricular Enlargement

Since the right ventricle is on the anterior surface of the heart, it does not appear on the heart border in the frontal view When the right ventricular chamber enlarges, it protrudes anteriorly toward the sternum As a consequence of this forward bulging of the right ventricular wall, the pulmonary artery

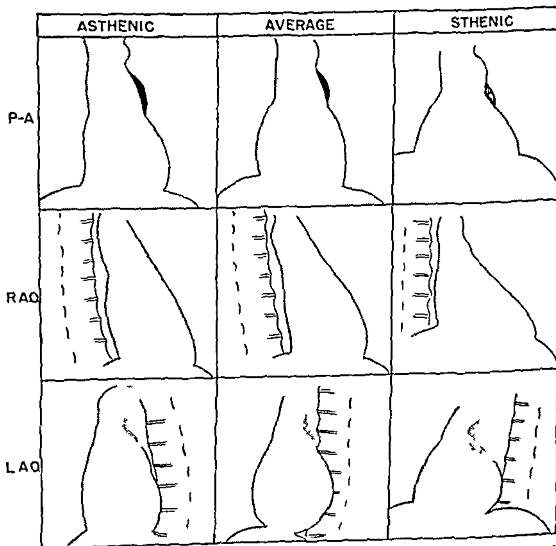


FIGURE 14 A dilated pulmonary artery appears on the left border of the mediastinal shadow in the frontal view It can be confirmed in some patients in the right anterior oblique view but is invisible in the left anterior oblique position

is displaced beyond the normal left border tending to obscure the cardiovascular angle[17,18] Thus the left border of the cardiac silhouette becomes straightened or even convex (Fig 13)

In the left anterior oblique position forward projection of the dilated right ventricular chamber produces a sharper angulation at its junction with the root of the aorta (Fig 13) In the right anterior oblique position the distance between the outflow tract of the right ventricle and the sternal shadow is reduced

Dilatation of the Pulmonary Artery

In certain types of congenital malformations of the heart the pulmonary artery becomes markedly dilated Such patients generally have an abnormally voluminous pulmonary blood flow The dilated pulmonary artery appears as a local prominent bulge just above the cardiovascular angle (Fig 14) This alteration in the cardiac silhouette is usually associated with a marked increase in the density of the pulmonary vascular markings particularly in the peripheral lung field Pulmonary valvular stenosis with dilatation of the pulmonary artery above the obstruction is a prominent exception to this rule (see Chapter 18)

It is not considered appropriate here to delve deeply into roentgenographic interpretation. Additional information concerning the finer details may be obtained from standard textbooks on the subject[19-21]

SUPPLEMENTARY ROENTGENOGRAPHIC TECHNIQUES

Angiocardiography

Since the blood and myocardium absorb x rays to a similar extent and the entire cardiac silhouette has relatively uniform density, the chambers cannot be differentiated from the walls By rapid injection of suitable radiopaque substances the blood can be opacified to a very great extent This technique is termed angiocardiography Serial roentgenograms taken in rapid succession after the injection of a contrast medium reveal the course of the blood through the cardiac chambers In the dog, the orientation of the heart within the thorax is well suited to angiocardiographic studies because each chamber of the heart may be visualized individually (see Figs 9 13, Chapter 1) Human angiocardiography, on the contrary, is seriously complicated by the fact that in any position, the individual cardiac chambers overlap Opacification of one area completely obscures all other structures superimposed upon it

The most common procedure is to inject Diodrast (70 per cent) or Neo-Iopax (75 per cent) rapidly into an antecubital vein Serial roentgenographic exposures are obtained at speeds of up to 8 per second Occasionally there are unpleasant side reactions to the contrast media including a hot flush headache vomiting, urticaria and syncope According to Dotter and Jackson[22] fatal reactions occur with an incidence of 0 38 per cent Angiocardiography should not be employed unless the risks are outweighed by the necessity for specific information in formulating definitive therapy This decision requires awareness of the types of cardiac lesions which are suitable for angiocardiographic study

The clinical application of angiocardiography has recently been reviewed by Dotter and Steinberg[23,24] Widespread interest has been evoked in the diagnosis of congenital malformations of the heart and great vessels including (a) coarctation of the aorta (b) complete transposition of the great arteries (c) aneurysm of the aorta as differentiated from mediastinal tumors (d) anomalies in the course of the aorta and its branching (e) anomalous drainage of pulmonary veins and (f) certain intracardiac defects (see Chapter 19) The technique has value in detecting specific pulmonary conditions (e g arteriovenous communications in the lungs)

The course of the radiopaque materials through the heart is generally recorded by the use of rapid cassette changers or roll film magazines[25] Cinefluorographic angiocardi-

shadow is composed of the right atrial margin superimposed upon the dilated left atrial chamber

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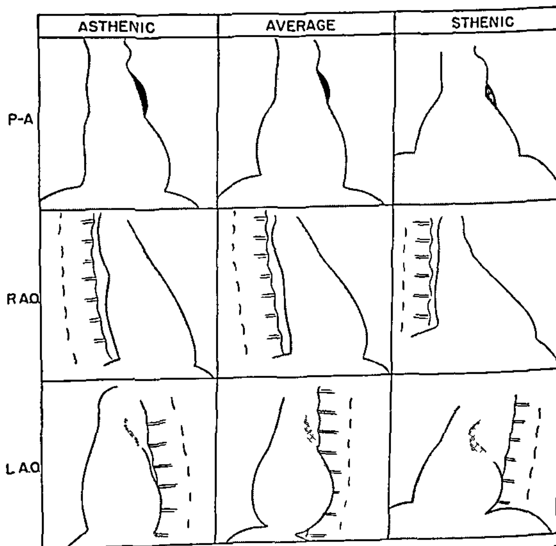


FIGURE 14 A dilated pulmonary artery appears on the left border of the mediastinal shadow in the frontal view It can be confirmed in some patients in the right anterior oblique view but is invisible in the left anterior oblique position

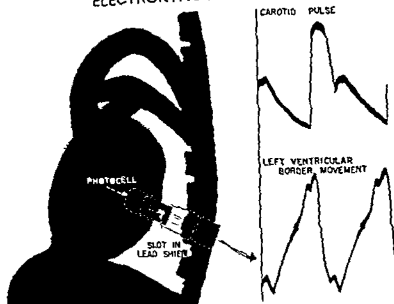


FIGURE 15 Electrokymographic recording is accomplished by positioning a photoelectric cell over the borders of the heart under fluoroscopic control. Within the recording head is a piece of lead with a rectangular slit covered by a small fluorescent screen. Roentgen rays striking the fluorescent screen, cause it to emit light in relation to the density of the intervening tissues. As the heart border moves back and forth across the slit, the quantity of light emitted by the fluorescent material varies providing an objective record of the motion of that portion of the heart wall.

With apparatus of this sort, changes in the density at the central portion of the ventricular chambers may be recorded and related to stroke volume Successfully accomplished this would represent a significant step in cardiovascular analysis since it would afford a simple method for continuously recording a function which appears closely related to cardiac output (see Chapter 12)

SUMMARY

Changes in size and shape of the heart are important signs of heart disease During early stages of heart disease the heart usually remains normal in size Detection of slight changes in the size of the cardiac chambers is extremely difficult because of variation in the size and shape of the normal heart due to orientation of the heart within the thorax the shape of the chest cage habitus age respiratory activity and other factors Extensive enlargement of the heart can be recognized with little difficulty by noting dislocation of the point of maximal impulse and by percussion Enlargement of individual chambers alters the configuration of the cardiac silhouette However, interpretation of roentgenograms requires experience in distinguishing individual variation of normal hearts from signs of chamber enlargement In each patient the cardiac silhouette must be considered in terms of the probable normal for that particular individual Supplementary techniques including angiocardiography and electrokymography provide additional information under particular circumstances but are not applicable to routine diagnosis

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ography is theoretically the method of choice because it provides a more complete coverage of the sequence of events. Repeated projection of the motion picture films reveals details which are entirely missed during examination of individual exposures. However, at the present stage of development, the adequate penetration requires high levels of radiation for periods of 10 seconds in adults and poses serious problems in obtaining high quality films without excessive radiation. Current developments in intensification of fluorescent images promise to solve many of these problems.

Roentgenkymography

During systolic ejection, the area of the cardiac silhouette is reduced so slightly that it is difficult to visualize the movements of the heart borders during fluoroscopy. Movements of the heart borders have been recorded by means of the roentgenkymograph.[6] The roentgenkymograph consists of a lead plate with a series of horizontal slits 1 cm. apart. Behind this grid a roentgenographic plate moves down 1 cm. at a controlled rate. Movements of the heart borders produce serrated margins on the cardiac silhouette. This apparatus has failed to achieve wide application for several reasons:[27] (1) the amplitude of the recorded movements of the heart borders is very small, (2) the exposure is limited to 1.0 to 1.5 seconds, (3) the slits are not always perpendicular to the heart border and (4) the diaphragmatic aspect of the heart is obscured by dense abdominal structures. In recent years a technique—electrokymography—has been developed to amplify the movements of specific points on the borders of the fluoroscopic image.

Electrokymography

The sensitive element of the electrokymograph is a photoelectric cell which responds to the light emitted by a small fluorescent screen mounted behind a long narrow slit in a rectangular piece of lead.[28, 29] Movement of the cardiac border back and forth along the slit during each cardiac cycle reduces the total number of x-rays reaching the small fluorescent screen and the total quantity of light striking the photoelectric cell (see Fig. 15). This process can be compared to holding a photographic exposure meter toward a window and recording the movements of the needle as a semi-opaque window shade is repeatedly raised and lowered. In this way, an objective record can be obtained which indicates the relative movements of the heart borders. It does not, however, distinguish between movements of the ventricular wall during contraction and changes in position of the heart within the thorax.

Electrokymography has been advocated for assessing a wide variety of clinical problems including the demonstration of paradoxical motion of the ventricular borders at the site of myocardial infarction. When a portion of the ventricular border moves outward during systole and inward during diastole, the presence of myocardial infarction is apparent. In constrictive pericarditis the filling is complete during early diastole, producing a pattern of very flat diastolic plateaus separated by V-shaped excursions due to systolic ejection and rapid filling. Varying degrees of success have been achieved in attempts to find distinctive patterns associated with myasthenia gravis, valvular disease and other forms of organic heart disease. The status of the method in 1950 was reviewed in detail in the proceedings of the first conference on electrokymography.[30]

Electrokymographs in current use were tested by Zinsser, Kay and Benjamin[31] and failed to produce instantaneous recordings which were directly proportional in magnitude to the dynamic event under study for three reasons: (*a*) the sensitivity of the phototubes was not uniform along the receptor slots, (*b*) a time lag (0.15 to 0.25 second) was observed and (*c*) the frequency response was inadequate. Morgan and Sturm[32] have described improved equipment which has sufficient stability and response to permit quantitative calibration.

Chapter 12

The Estimation of Cardiac Output

Since cardiac reserve can be evaluated only by determining the cardiovascular response to a load a method for directly measuring cardiac output during exertion would be very valuable in cardiac diagnosis and prognosis Unfortunately, direct measurements of cardiac function in man although desirable are virtually impossible because the heart is quite inaccessible for determining either stroke volume or absolute volume Perhaps the most direct method is the calculation of changes in cardiac volume from the cardiac silhouette on roentgenographic plates [1,2] However this method has serious limitations because the individual cardiac chambers cannot be differentiated on routine roentgenograms so the computed values represent the total volume of all four *chambers* In recent years a wide variety of techniques has been proposed to determine cardiac output by indirect methods The basic principles and limitations of some of the techniques currently in vogue will be described

THE FICK PRINCIPLE

Blood flow through an organ can be determined if a substance is either removed from or added to the blood during its flow through the organ Applied to the lungs the Fick principle is used to calculate the volume of *blood required* to transport the oxygen taken up from the alveoli per unit time The fundamental concept is deceptively simple and can be illustrated schematically by representing the oxygen-carrying capacity of the blood as beakers on a conveyer belt (Fig 1)

Measurement of Oxygen Consumption

Of necessity the oxygen consumption is generally measured over a period of several minutes The accuracy of oxygen uptake determinations from the clinical B M R. apparatus is generally inadequate for this purpose A preferred technique consists of collecting in a spirometer all of the air expired during carefully timed intervals and analyzing samples for oxygen content (Fig 2) Comparing the oxygen content of the total exhaled volume with a similar volume of ambient air provides the data *required to* compute the oxygen uptake accurately

The Arteriovenous Oxygen Difference

The arterial blood throughout the body normally has a uniform oxygen content However to determine a significant A-V oxygen difference it is necessary to obtain samples of *mixed* venous blood The quantity of oxygen contained in venous blood

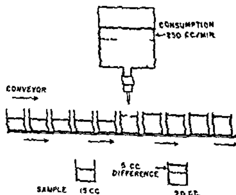


FIGURE 1 If each beaker on a conveyer belt receives 5 cc of fluid as it passes under a dispenser delivering 250 cc. per minute the beakers must pass the dispenser at a rate of 50 per minute (250/5) to carry that quantity of fluid. Similarly if each 100 cc. of blood takes up 5 cc. of oxygen from the lungs (A V oxygen difference) and 250 cc. of oxygen are consumed each minute, 50 increments of 100 cc (5000 cc.) of blood must have passed through the lungs each minute This is the Fick principle as it is applied to the calculation of cardiac output (see Fig 2)

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simultaneously in two different spectral regions approximately 750 to 900 millimicrons and 600 to 750 millimicrons respectively. The former is near infra red light in wave length and is transmitted by both oxyhemoglobin and reduced hemoglobin to approximately equal degrees. The other photocell responds to red light which is transmitted well by oxyhemoglobin and to a very slight degree by reduced hemoglobin. The ratio between the light intensities recorded from the two wave lengths can be read in terms of absolute percentage of oxygen saturation after the apparatus has been satisfactorily calibrated by means of Van Slyke analysis. In experienced hands this device more than makes up for the slight reduction in accuracy through the ease with which serial determinations can be obtained in rapid sequence while the patient is under study.

Sources of Error

The conventional expression of the Fick principle $F = (\text{oxygen consumption})/(\text{A-V oxygen difference})$ presupposes that these values are obtained simultaneously *and are* constant during the time of measurement. Both the cardiac and the respiratory cyclic activity may exhibit changes and introduce errors in cardiac output calculations. Even if blood samples are drawn continuously or repeatedly during the determination of oxygen consumption they represent time averages not volume averages. The factors which may cause errors in sampling and computations of cardiac output have recently received considerable attention.[10,11] Under resting conditions the A-V oxygen difference is probably fairly constant. During inhalation of low oxygen mixtures serious errors may be encountered. Shunts between the pulmonary and systemic circuits also induce rather large errors in the calculation of systemic flow. Special formulas have been developed to calculate the volume flow of blood through such shunts.[6]

The accuracy of cardiac output determinations depends upon the cumulative magnitude of the errors in sampling and analysis of the blood oxygen content and oxygen consumption.[5,12] It is generally stated that the cardiac output determined by the direct Fick method has an accuracy of ± 10 per cent. This is true when groups of data are averaged, but the error may be considerably greater in an individual case.

A test which may produce an alteration in

THE CUVETTE OXIMETER

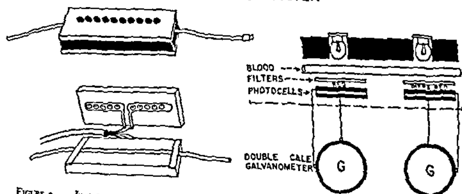


FIGURE 3 In a cuvette oximeter a polyethylene catheter containing the blood specimen lies between a row of light bulbs and photocells equipped with filters. Red light is well transmitted by oxyhemoglobin and largely absorbed by reduced hemoglobin, so changes in the oxygen content of the blood affect the output of the photocell with a red filter. The second photocell is covered by a filter transmitting infra red light which is absorbed to approximately the same degree by both oxyhemoglobin and reduced hemoglobin. The quantities of light reaching the two photocells are recorded by means of a double scale galvanometer. (From Groom D, Wood, E H, Burchell H B and Parker R. L. The application of an oximeter to diagnostic cardiac catheterization. Proc. Mayo Clin. 23 601-609 1948.)

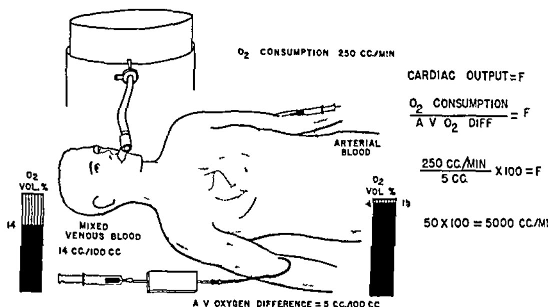


FIGURE 2 Computing cardiac output according to the Fick principle requires simultaneous determin tion of oxygen consumption and the arteriovenous oxygen difference Exhaled air is collected to measu oxygen consumption per minute By withdrawing blood from the pulmonary artery through a catheter in a cuvette oximeter the oxygen content of mixed venous blood can be read from a galvanometer (see Fig 3 Arterial oxygen content is measured in a sample of blood from any systemic artery The A V oxygen differen in cubic centimeters of oxygen per 100 cc. of blood is obtained by subtracting the oxygen content of t mixed venous sample from the arterial oxygen content

depends upon the vascular bed from which it is returning (see Fig 3, Chapter 5) For example, blood from the kidneys and skin remains highly saturated with oxygen while blood from the coronary vessels and exercising muscle is largely depleted of oxygen The oxygen contents of venous blood from other tissues vary between these extremes Due to laminar flow in the venous channels currents of blood with a relatively high oxygen content may accompany streams with lower values in the same vein The oxygen saturation of blood in the superior vena cava differs from that in the inferior vena cava and these two streams of blood do not mix completely within the right atrium The Lipiodol streamers in Figure 10, Chapter 1, graphically illustrate this fact Mixing of blood does occur in the right ventricle and is generally complete by the time the blood has entered the pulmonary arteries A sample of mixed venous blood, obtained from the pulmonary artery, represents an average of the venous oxygen content which can be used to establish the arteriovenous oxygen difference for calculating cardia output by the Fick principle

CARDIAC CATHETERIZATION In 192 Forssmann[3] demonstrated that a cathet can be passed through the venous channe into the right chambers of the human hea (Fig 2) Cournand and his associates[4] established the safety of the procedure an stimulated widespread utilization of th method The technique of cardiac catheteri zation has been described in detail by Cour nand,[6] Warren,[7] Sosman[8] and Dexter [9]

MEASUREMENT OF BLOOD OXYGEN CON TENT Arterial and venous oxygen conten can be directly measured with the Va Slyke apparatus, which is a time-consuming but accurate procedure in the hands of highly qualified technicians For rapid determinations of blood oxygen content a photoelectric method has been developed and compares favorably with Van Slyke determinations Blood for analysis is drawn through a cuvette oximeter (Figs 2, 3), where it is transillu minated by a constant intensity light source and the transmitted light is registered

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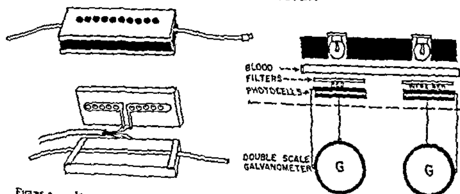


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the factor being measured must be carefully controlled From the patient's point of view, cardiac catheterization is a rather heroic procedure which may give rise to considerable apprehension The possibility that cardiac output is abnormally increased to a variable extent during catheterization must be constantly considered

Objective determinations of cardiac output have been of great value in advancing our knowledge of circulatory dynamics, with particular reference to pulmonary function in health and disease However, the search *for an objective test of cardiac reserve* was not ended by the development of cardiac catheterization, because the procedure is too complicated for routine clinical use and is not entirely suitable for use during strenuous exertion A normal value for cardiac output at rest is often obtained when the cardiac reserve is seriously depleted

Additional Information from Cardiac Catheterization

If cardiac catheterization provided no information beyond the resting cardiac output, its utilization would be largely limited to fundamental investigation However, several additional types of information can be gained from catheterization which are particularly useful in the diagnosis of congenital malformations of the heart (see also Chapter 19)

DEFECTS IN THE PARTITIONS OF THE HEART A sample of blood withdrawn from a catheter lying in the pulmonary artery may contain more oxygen than that measured from the right ventricle This situation exists in patients with patent ductus arteriosus or aortic septal defects Similarly, if the oxygen content of the blood within the right ventricle significantly exceeds that in the inferior or superior vena cava or right atrium, a defect in the interventricular septum should be suspected Defects in the partitions of the heart may also be directly demonstrated by passing the tip of the catheter through the defect into the systemic side of the circulation (see Chapter 19)

DETECTING OBSTRUCTION IN VASCULAR CHANNELS The external end of the catheter may be connected to a suitable pressure recording device The pressures in the pulmonary artery and right ventricle can then be recorded as the catheter is withdrawn Normally, the gradient in systolic pressure between the right ventricle and the pulmonary artery is so small it defies detection Impedance to pulmonary blood flow in the form of pulmonary valvular or infundibular *stenosis in the right ventricular outflow tract* can be identified when there is a large pressure gradient between the right ventricular chamber and the pulmonary artery (see Fig 11, Chapter 18)

PRESSURES FROM CATHETERS WEDGED IN TERMINAL PULMONARY ARTERIAL BRANCHES The tip of a cardiac catheter can be advanced into the pulmonary arterial system until it becomes impacted in a terminal arterial branch Through the orifice in the tip of the catheter, pressure fluctuations can be recorded from regions beyond the catheter (see Fig 8, Chapter 18) Such pressures are frequently termed "pulmonary capillary pressure " Since the pressure gradient in the pulmonary circuit is normally very slight, such wedged-catheter pressures are often considered to indicate left atrial or even left ventricular diastolic pressure In fact, such pressures have been employed to compute the area of the mitral orifice in patients with mitral stenosis Such calculations involve assumptions which are not necessarily sound and the derived numerical values may have rather great errors Values for pulmonary resistance have also been calculated using wedged-catheter pressures and assuming that left ventricular diastolic pressure is negligible, a dubious assumption indeed Burton[13] discussed the value and misuse of wedged-catheter pressures and advanced compelling arguments against 'spoiling a scientific measurement by building upon it such a house of cards, the deceptive facade

of which may well mislead the trusting clinician into buying it

CORONARY SINUS CATHETERIZATION The catheter has been inserted into the coronary sinus to withdraw blood which has supplied the myocardium[14] From samples of this type it has been possible to calculate the oxygen consumption and myocardial efficiency of the left ventricular myocardium (see Chapter 8)

THE STEWART PRINCIPLE

The volume of fluid in a container can be calculated by adding a known quantity of dye and measuring the concentration of the material after it has become evenly dispersed through the fluid (Fig 4A) The volume is calculated according to the formula $V = A/C$, where V is the volume of fluid, A is the amount of dye added and C is the concentration of the dye in each cubic centimeter of the fluid Stewart[15,16] demonstrated that this method can also be applied to fluids in motion Hamilton and his associates[17,18] verified the usefulness of the method in calculating the flow through glass models and in the circulation Moore et al[19] obtained a good correlation between the dilution method and the direct Fick method

General Principles

The computation of a volume of stationary fluid by determining the dilution of a known quantity of dye is perfectly straightforward

THE INDICATOR DILUTION TECHNIQUE

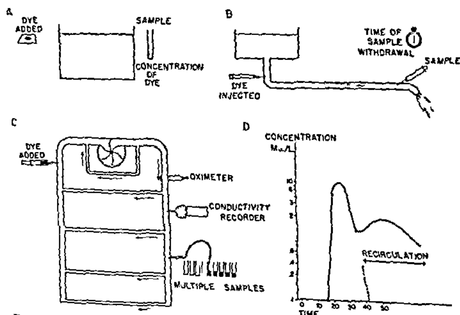


FIGURE 4 *A* The volume of stationary fluid in a reservoir can be determined by completely mixing a known amount of dye and analyzing a sample for the concentration of the dye

B The volume flow through a simple tube can be estimated by injecting a known quantity of dye withdrawing a sample at constant rate during the passage of the dye-containing fluid and determining the mean concentration of the sample

C A hydraulic model simulating the circulatory system illustrates the fact that an indicator substance may pass through short circuits and begin to recirculate before the mass of dye has passed the sampling point. Therefore it is necessary to devise means by which the amount of recirculating dye can be separated from the amount of dye sampled during its initial passage to arrive at a reliable mean concentration

D If the concentration of the dye passing a sampling point is plotted on semi log paper the descending limb after the peak can be extended to the baseline as a straight line. The area under the initial curve can be used to derive the mean concentration of the dye during its first circulation.

(Fig 4) Similarly, the volume flow through a simple tubular system can theoretically be determined with considerable accuracy by determining the average concentration of a known quantity of dye and the time during sampling according to the formula $F = A/Ct$, where F is flow, A is quantity of dye injected, C is the average concentration of dye in the sample and t is the duration of sample withdrawal (Fig 4*B*) Under these conditions, the Stewart principle is quite as accurate as the Fick principle However, conditions in the human circulation are more complex, as indicated by the hydraulic model in Figure 4*C* Part of the dye injected at one point in *this model has completely traversed the* short circuits and begun to recirculate before the material has reached the more distant *regions The average concentration of the* indicator substance can be measured by (1) collecting multiple samples in rapid succession, (2) continuously recording blood conductivity after saline injections or (3) making oximeter or densitometer recordings when dyes are injected In any case, the concentration of indicator flowing past the point of recording reaches a peak, begins to descend and then increases again owing to recirculation If the once-circulated dye can be separated from the recirculated dye, cardiac output can be computed with considerable accuracy

One of the techniques originally described by Stewart[16] included the following steps A control sample of blood was withdrawn Hypertonic salt solution was then injected The arrival of the increased concentration of salt in a peripheral artery was signalled by a change in the tone from a telephone connected to a Wheatstone bridge, one leg of which responded to a change in the conductivity of the blood in the artery A single sample of blood was then collected from the peripheral artery throughout the entire interval during which the mixture was passing the collecting cannula To determine the concentration of the injected salt solution in this sample, the control sample was titrated with the same salt solution until the conductivities of the two samples were identical Note that the only difference between the *formula for determining the volume of fluid* in a container ($V = A/C$) and the formula for volume flow ($V = A/Ct$) is the factor of time (t) during which the sample is collected

The fundamental requirements for this method are (1) the injection of a material which can be accurately analyzed and which does not leave the blood during the test, and (2) a sample of arterial blood which indicates the average concentration of the material during its first circulation through the arterial tree Various dyes as well as saline solutions have been used with varying degrees of success and the average concentration has been determined by either repetitive sam*pling or by continuous recording*

Accuracy of the Indicator Dilution Technique

Hamilton and Remington[17,20] demonstrated that when a foreign substance is injected into a vein at a constant rate, it begins to recirculate before a concentration plateau is established They warned against the use of diffusible substances, some of which may be lost during passage through the heart and lungs, and urged the use of dyes such as T-1824 (Evans blue) which *tend to remain in the blood stream*

In addition to errors in collecting and measuring samples and in determining the time intervals Stewart[15] discussed the following sources of error (1) incomplete mixture of the solution with the blood (2) variations in velocity in the central and peripheral laminae in blood vessels (3) loss of blood from sampling and (4) dilution of the blood by large injections He felt that the errors from these sources were *not serious* Wiggers[21] has described important refinements of the procedure which should improve its accuracy White[22] developed a method for continuously recording the conductivity of blood during saline injections so that repeated determinations can be made with less effort

PRESSURE PULSE CONTOUR METHOD

The Relation of Pulse Pressure to Stroke Volume

Erlanger and Hooker[23] recognized that the product of the pulse pressure and the heart rate indicated cardiac output, with the following reservations In order to be able to obtain a knowledge of the absolute velocity of blood flow from a knowledge of the pulse-pressure and pulse rate it is necessary to know

1 The rate of systolic output For if a given amount of blood be driven into the aorta with different rates the maximum pressure would be higher when this rate is rapid than when it is slow

2 The rate of flow from the arteries into the veins For this flow continues during cardiac systole and consequently variations in the rate of this flow would vary the height to which the force of the heart would raise the systolic pressure

3 The distensibility of human arteries at different pressures The distensibility diminishes as the pressure increases consequently at a high pressure it would require a smaller systolic output to produce a pulse-pressure of a given magnitude than at a low pressure

4 The amount of blood in the systemic arteries under various conditions The fall of pressure during diastole depends upon the relative amount of blood that escapes into the veins not upon the absolute amount

We do not know how large any one of these factors is but it seems probable that under more or less normal conditions none of them would produce a very large error Upon this assumption we are perhaps justified in using the product of the pulse pressure by the pulse rate as an index to the relative velocity of blood flow

Clearly the stroke volume would be directly proportional to arterial pulse pressure only if the pressure volume relations of the arterial system were not only constant and uniform among individuals but linear from high pressure to low That this is not the case has been emphasized previously (see Chapters 2 and 10) However, the blood pressure is controlled and if the differences in arterial distensibility were not too great, a reasonable approximation of stroke volume could be determined from the pulse pressure Remington[24] presented a set of volume factors from known stroke volumes and pulse pressures corrected for body size and distensibility curves From this table stroke volume/sq m body surface could be predicted with an error of about 25 per cent According to Hamilton and Remington[5] pulse pressure correlates roughly with stroke volume determined by the dye dilution technique ($r = 0.88$) Over the normal pressure range, a pressure rise of 1 mm Hg was equivalent to about 1 cc of stroke volume/sq m For some purposes this degree of accuracy might be quite sufficient However a great deal of effort has been expended in attempts to increase the precision with which stroke volume is derived from the pressure-pulse contour This is no simple matter considering the complexity of the situation

Analysis of Pulse Contours

If fluid is injected into a distensible container with fixed volume elasticity the volume in the system can be calibrated in terms of the internal pressure (Fig 5) Once the volume pressure relations are established the volume contained can be determined by noting the pressure in the system However, if fluid can escape from the system (Fig 5) the elastic chamber will remain distended only if fluid is pumped in at the same average rate as it leaks out Under these circumstances, the pressure will increase as the chamber is distended and decrease between pumping strokes as the fluid leaves the system The difference between the maximal and minimal pressures indicates the amount of fluid injected at each stroke less the amount which left the system during the ejection period If the distensible chamber is a long narrow cylinder with elastic walls the fluid ejected by the pump is not instantaneously distributed through the sys-

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PRESSURE PULSE CONTOUR METHOD

The Relation of Pulse Pressure to Stroke Volume

Erlanger and Hooker[13] recognized that the product of the pulse pressure and the heart rate indicated cardiac output, with the following reservations In order to be able to obtain a knowledge of the absolute velocity of blood flow from a knowledge of the pulse-pressure and pulse rate it is necessary to know

1 The rate of systolic output For if a given amount of blood be driven into the aorta with different rates the maximum pressure would be higher when this rate is rapid than when it is slow

2 The rate of flow from the arteries into the veins For this flow continues during cardiac systole and consequently variations in the rate of this flow would vary the height to which the force of the heart would raise the systolic pressure

3 The distensibility of human arteries at different pressures The distensibility diminishes as the pressure increases consequently at a high pressure it would require a smaller systolic output to produce a pulse-pressure of a given *magnitude* than at a low pressure

4 The amount of blood *in* the systemic arteries under various conditions The fall of pressure during diastole depends upon the relative amount of blood that escapes into the veins not upon the absolute amount

"We do not know how large any one of these factors is but it seems probable that under more or less normal conditions none of them would produce a very large error Upon this assumption we are perhaps justified in using the product of the pulse pressure by the pulse rate as an index to the relative velocity of blood flow

Clearly the stroke volume would be directly proportional to arterial pulse pressure only if the pressure volume relations of the arterial system were not only constant and uniform among individuals but linear from high pressure to low That this is not the case has been emphasized previously (see Chapters 2 and 10) However the blood pressure is controlled and if the differences in arterial distensibility were not too great a reasonable approximation of stroke volume could be determined from the pulse pressure Remington[4] presented a set of volume factors from known stroke volumes and pulse pressures corrected for body size and distensibility curves From this table stroke volume/sq m body surface could be predicted with an error of about 25 per cent According to Hamilton and Remington[5] pulse pressure correlates roughly with stroke volume determined by the dye dilution technique ($r = 0.88$) Over the normal pressure range, a pressure rise of 1 mm Hg was equivalent to about 1 cc of stroke volume/sq m For some purposes this degree of accuracy might be quite sufficient However a great deal of effort has been expended in attempts to increase the precision with which stroke volume is derived from the pressure-pulse contour This is no simple matter considering the complexity of the situation

Analysis of Pulse Contours

If fluid is injected into a distensible container with fixed volume elasticity the volume in the system can be calibrated in terms of the internal pressure (Fig 5) Once the volume pressure relations are established the volume contained can be determined by noting the pressure in the system However if fluid can escape from the system (Fig 5) the elastic chamber will remain distended only if fluid is pumped in at the same average rate as it leaks out Under these circumstances, the pressure will increase as the chamber is distended and decrease between pumping strokes as the fluid leaves the system The difference between the maximal and minimal pressures indicates the amount of fluid injected at each stroke less the amount which left the system during the ejection period If the distensible chamber is a long narrow cylinder with elastic walls the fluid ejected by the pump is not instantaneously distributed through the sys-

THE PULSE CONTOUR METHOD

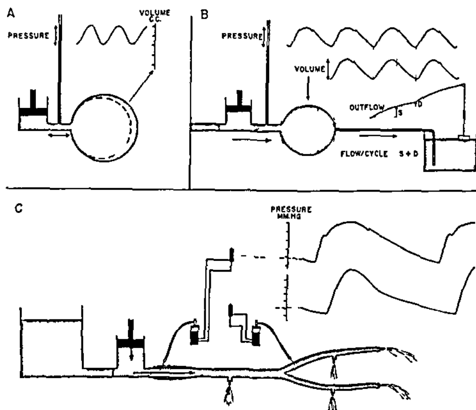


FIGURE 5 *A* The changes in the volume of the balloon can be determined by measuring the pressure if the pressure volume relations are constant

B If fluid is pumped into a balloon and flows out through a tube offering some resistance the flow through the system can be estimated from the pressure fluctuations The volume and pressure within the balloon increase during ejection from the pump but outflow occurs throughout the entire cycle Using pressure fluctuations to indicate changes in volume the flow from the system can be estimated by determining the flow out of the system during diastole (D) and adding a computed value for outflow from the system during the stroke (S)

C In the circulatory system the pulse of pressure does not reach all parts of the elastic pressure reservoir simultaneously and its contour changes as it passes through the system (see also Fig 3 Chapter 10) Under these conditions the volumes entering and leaving various portions of the system must be considered individually to reach maximum accuracy Since this is not practical in intact animals or man the computation of cardiac output from pressure pulses has been greatly simplified However each step toward simplification of the method involves sacrifice of accuracy

tem and the recorded pressure will be distorted by reflected waves A similar situation obtains within the arterial system of the body (see Fig 3, Chapter 10)

Hamilton and Remington[25] recognized that prediction of stroke volume from pressure pulses must depend upon evaluation of the 'individual arterial distensibility, knowledge of the pulse pressure in the arterial tree and its several parts, and the estimation of *arteriolar drainage* " They *developed a table* indicating the capacity of the various portions of the arterial tree at different pressures and another showing the pulse wave transmission times to the parts of the arterial tree at various diastolic pressures These data *were employed in the analysis of* pressure pulses A very good correlation with the dye dilution method (0 994) was found when the stroke volume computations were based upon details of the pressure pulse contours, trans mission times to the various parts of the arterial tree and the distensibility of those parts Remington et al[26] and Warner[27] subsequently reported a simplified technique *which facilitates analysis of the* pressure pulse with little increase in the error In spite of these favorable results Wiggers[28] stated "While the published data do not lend themselves to statistical analysis, they

certainly do not demonstrate that the pulse contour method is reliable for determining the cardiac index in serial determinations on a given animal ' In spite of this rather dim view the pulse contour method has one very important potential advantage It permits computation of the stroke volume of individual cycles even though its accuracy may be limited.

BALLISTOCARDIOGRAPHY

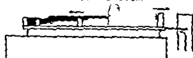
The concept that a sudden motion of the blood in one direction must produce a recoil of the body in the opposite direction is not a new idea In 1887 Gordon[29] compared the ballistic forces of the body to the recoil of a gun In 1905 Henderson[30] used a swinging table to record the movements along the longitudinal axis of a patient reclining on its surface The changing velocity of the moving blood within the circulatory system caused the table to oscillate during each successive cardiac cycle

General Principles

The recoil of a rifle is frequently employed as an analogy for explaining the basic principles of ballistocardiography If a rifle is rigidly fastened on a spring mounted table a discharging cartridge propels the bullet out of the barrel and displaces the rifle in the opposite direction (Fig 6A) Recording the movements of the table under these circumstances might provide information concerning the magnitude of the powder charge (energy release) if other conditions are known If the magnitude of the powder charge and the muzzle velocity were unknown the weight of the bullet (mass ejected) could not be computed from the

BALLISTOCARDIOGRAPHY

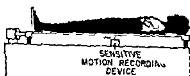
A RECOIL OF RIFLE AND BULLET



B RECOIL OF HEART AND BLOOD



C BALLISTOCARDIOGRAPH



D COUPLING



E. BALLISTOCARDIOGRAM

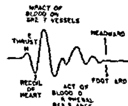


FIGURE 6 *A* The recoil of a rifle during discharge of a cartridge can be recorded by attaching it rigidly to a spring-mounted table The record would become seriously distorted if the bullet ricocheted from a barrier on the table during the recoil of the rifle

B The blood ejected by the ventricles travels in several directions simultaneously imparting its energy to the body at every turn. For this reason, measurements of the recoil of the body in one direction only are inadequate

C A low-frequency spring mounted table which has been critically damped has been recommended for ballistocardiography because the body cannot be rigidly fastened to the table. The tissues in contact with the table have an elasticity which is equivalent to interposing a spring between the body and the table top

D If the springs supporting the table are stiff in relation to the elasticity of the tissues the recorded patterns tend to reflect the elastic properties of the tissues supporting the body as the forces are imparted by the heart and blood.

E Ballistocardiographic records consist of a series of deflections which have been related to the events of the cardiac cycle. Although the forces developed by the heart and blood affect the recorded patterns a consistent relationship between these deflections and stroke volume is probably fortuitous for the most part

recorded deflections. The analysis would be seriously complicated if, during the recoil of the rifle, the speeding bullet struck a steel plate mounted on the same table. Since the blood does not leave the system, the recoil of the heart and body from ejection of blood into the arteries is even more complex. For example, the blood ejected from the two ventricles moves simultaneously in several directions after leaving the heart. Its energy is imparted to the body at every turn. Routine ballistocardiograms indicate movements of the body in only one direction. Simultaneous recordings in three dimensions are extremely difficult to analyze. Finally, the records may be seriously distorted by such factors as the coupling between the body and the table. The elasticity of the skin acts as a spring interposed between the moving body and the table top, and may have a profound influence on the recorded deflections. This difficulty can be alleviated by recording from patients on a light table floating on a layer of mercury,[31] but this is not a practical solution.

Evaluation of Ballistocardiography

Starr and his associates[32] extended the observations of Henderson and reawakened interest in the recoil phenomena by stating that the size of the initial waves, I and J, is related to the cardiac output, and that the form of the ballistic curve is determined by the shape of the curve of blood velocity in the great vessels.[33] Dow and Hamilton[34] studied the recoil of models simulating the circulation and concluded that the form and frequency of the recorded waves are associated with the standing waves in the "aorta" of the model (see Fig. 3, Chapter 10). Actually, the size of the initial deflection is determined by the acceleration of the fluid (the rate at which velocity of ejection is built up) and not at all by the total stroke output. Nickerson and Curtis[35] demonstrated that with high frequency apparatus of the type used by Starr, the size and shape of the deflections is determined almost completely by the elastic properties of the skin (the coupling between the body and the table). For this reason, critically damped ballistocardiographic apparatus with very low frequency (less than 1.5 c.p.s.) produces much more reliable records. Using a simple, low frequency ballistocardiograph, Hamilton et al.[36] demonstrated that the mass of the body itself renders the ballistocardiograph an imperfect recorder of rapid oscillations. The recorded oscillations are the resultant of vascular and body movements as they may be in phase and reinforce one another, or be out of phase and cancel each other. Reconstruction of the ballistocardiographic records led to the following description of the causes of the various oscillations. The H wave begins with movements that take place during isometric contraction and are the most variable. The I wave is the result of a partly cancelled footward thrust developed as blood is ejected from the heart into the ascending aorta and pulmonary artery. The J wave has a complex origin, including the deceleration of blood in the heart, ascending aorta and pulmonary artery, and the acceleration of blood in the descending aorta. Although the usual ballistocardiogram represents movements along the longitudinal axis of the body, the generated forces are actually in three dimensions. For example, the I wave is the resultant of forces acting toward the left, ventrad and caudad. This is reasonable considering the orientation of the heart within the thorax. The calculation of cardiac output from ballistic waves is an empirical procedure which cannot give values with inherent validity.

Currently simplified ballistocardiographic apparatus is receiving extensive clinical use.[37] The obvious limitations of the method do not preclude the recognition of empirical relationships between various types of cardiac dysfunction and characteristic ballistocardiographic patterns. Since the amplitude of the deflections is influenced by the rate at which blood is accelerated, variations in the

pattern should reveal alterations in the force of ventricular ejection

SUMMARY

Cardiac output can be determined through the use of cardiac catheterization according to the Fick principle The theory is basically sound The accuracy of the determinations depends upon the cumulative errors caused by deviations from the steady state conditions required for application of this theory Very significant errors result whenever respiratory or circulatory conditions are inconstant

The indicator dilution technique is also basically sound for computing flow through simple tubular systems In the circulatory system application of the Stewart principle is complicated by problems related to recirculation of the indicator With proper precautions this technique affords values comparable to those derived from cardiac catheterization

Theoretically stroke volume can be determined from an analysis of the arterial pulse contour However many sources of error are present including intangible factors such as differences in arterial distensibility among individuals If the pulse contour method can be calibrated by the Fick principle in a particular subject, it becomes much more reliable If the magnitude of the potential errors is recognized the pulse contour method has considerable practical value since stroke volume of individual cycles can be estimated

Ballistocardiography has been widely used to compute values presumed to represent stroke volume or cardiac output Reliable recordings of body movements in response to ballistic forces during the cardiac cycle may be related to the rate or force of ventricular ejection but even the basic principles of the method fail to reveal any direct relationship between the magnitude of the deflections and the volume of blood ejected This fact does not preclude the establishment of empirical relations between specific ballistocardiographic patterns and certain forms of cardiovascular disease

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Chapter 13

Heart Sounds and Murmurs

Auscultation is the most sensitive test of the functional integrity of the heart. Frequently murmurs or alterations in the heart sounds are the only definite signs of organic heart disease, appearing long before the stress on the cardiovascular system is sufficient to produce other signs and symptoms. As in any sensitive test of physiologic function the distinction between normality and abnormality is difficult in many borderline cases. Nevertheless characteristic murmurs and changes in heart sounds may direct attention toward the heart as the site of disease processes. In a few conditions a distinctive murmur provides a definite diagnosis of an anatomic lesion at an early stage in its development. Clinicians learn to recognize well developed characteristic murmurs by training and experience. However the significance of murmurs and the subtle changes in heart sound can be more fully appreciated with a fairly clear understanding of the nature of the sounds, the mechanics of sound transmission and the characteristics of auditory perception.

THE NATURE OF SOUNDS

Production of Sounds

Sounds are subjective interpretations of the sensations produced by the vibrations reaching the auditory apparatus. Sound waves are produced and transmitted by the vibratory motion of particles or bodies which are repetitively displaced from their position of equilibrium and then restored by a force of restitution toward their position of rest (Fig 1*A*).

Characteristics of Sounds

Consider a vibrating tuning fork with its prongs vibrating simultaneously (Fig 1*B*). During the time that the right prong moves toward the tube the air molecules are compressed at the orifice. A wave of compression moves through the tube with the velocity of sound in air (1100 ft per second). When the prong moves back, the air molecules rush back to fill the void and a wave of rarefaction follows the compression wave at that same velocity down the tube.

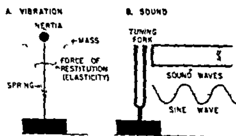


FIGURE 1. *A* Vibration occurs when a mass held in position by elastic support, is displaced from its position of rest. The spring tension acts to return the mass toward the equilibrium position but momentum carries it beyond the position of rest. An oscillatory motion of the mass back and forth past the position of rest persists until the energy instilled in the system is dissipated by friction.
B Sound waves produced by a tuning fork are waves of alternating compression (increased pressure) and expansion (reduced pressure) of the air. The fluctuating pressures from a vibrating tuning fork are recorded from a microphone as a sine wave indicating that the sound is a pure tone.

FREQUENCY. The frequency at which a system vibrates depends upon the mass in motion in relation to the restoring force (elasticity). A small mass fastened to a stiff spring vibrates rapidly (Fig 2*A*). These factors were discussed previously in relation to pressure recording devices (Chapter 10). In general the mass of body tissues is large in relation to their elasticity, so they tend to vibrate at low frequencies.

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fore the A V valves are closed) The exact cause of these initial vibrations has been controversial[2,5] The second component of the first heart sound consists of more intense vibrations beginning just as the ventricular pressure starts to rise signaling the closure of atrioventricular valves The third component resembles the second component in frequency and intensity[6,7] and occurs as the ventricular walls begin to contract However contraction of myocardial fibers is probably not the immediate cause of these vibrations[8,9] The fourth component of the first sound occurs during rapid ejection of blood from the ventricles into the corresponding arteries Only the second and third components of the first sound are consistently audible

The second heart sound has also been divided into four components,[10] although they may not all appear on a single phonocardiogram The initial vibrations have slight intensity and are inaudible The second component consists of a few high amplitude vibrations which represent the audible portion of the second sound These vibrations are clearly associated with closure of the semilunar valves The third and fourth components are small and unimpressive

The third heart sound consists of a few low-frequency vibrations occurring in early diastole Although such deflections can be recorded consistently[11,12] the third heart sound is heard rarely in normal adults It is perceived somewhat more frequently in children The third heart sound occurs at the end of the rapid filling phase and its intensity is affected by the rate of ventricular filling[13]

Since the major components of both the first and the second heart sounds are apparently associated with closure of the atrioventricular and semilunar valves respectively, it is appropriate to consider the anatomy and function of these remarkable structures

THE FUNCTIONAL ANATOMY OF HEART VALVES

The heart valves are so simple and effective that the best available man made sub-

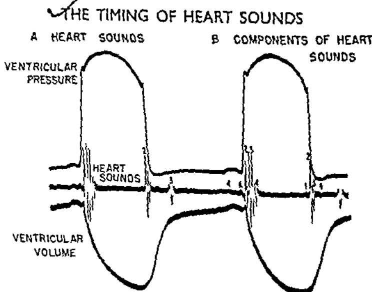


FIGURE 3 A Four heart sounds may be recorded during each cardiac cycle in some subjects The audible vibrations of the first heart sound appear at the beginning of ventricular systole coincident with the rise in ventricular pressure The second heart sound is associated with the dicrotic notch on the pressure curve (closure of the semilunar valves) The third heart sound occurs at the end of the rapid filling phase during ventricular diastole The fourth heart sound is associated with atrial contraction.
B Both the first and second heart sounds are sometimes divided into four components the causes of which are discussed in the text (see also Fig 10)

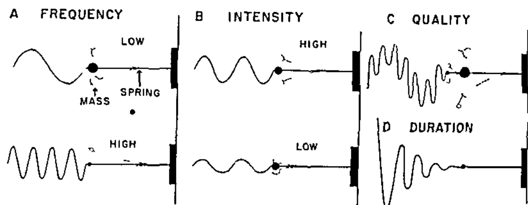


FIGURE 2 *A* The frequency of vibration (cycles per second) is determined by the relation between the mass and the elasticity of its support a large mass on a weak spring produces a slow vibration a small mass on a stiff spring vibrates rapidly

B The amplitude of vibrations depends on the amount of displacement from the position of rest (the energy imparted to the system)

C The quality of vibrations refers to the number of overtones or harmonics which are schematically represented by two vibrating systems connected in series When responding to complex sounds a single structure may be simultaneously vibrating at more than one frequency (e g the cone of a loudspeaker)

D The duration of a vibration after the source of energy is cut off depends upon the rate at which the energy is dissipated The greater the frictional resistance to motion the faster the energy is used up and the greater the damping

rule are bones and connective tissue structures under high tension (e g , arterial walls)

INTENSITY The intensity of the sound waves depends upon the amplitude of the vibrations, which is determined by how far the vibrating body is displaced In other words, the intensity of the sound depends upon the amount of energy imparted to the vibrating body as it is displaced from its position of rest (Fig 2*B*)

QUALITY A tuning fork is an instrument *that produces a pure tone, a sound with but* one frequency which is recorded as a sine wave (Fig 1*B*) Most natural sounds are composed of various frequencies or overtones which combine to determine the quality of the sound (Fig 2*C*) Distinctive combinations of tones and harmonics allow recognition of different musical instruments, of familiar voices, or characteristic heart sounds The vibrations emitted by the heart should be classed as noises since they are composed of unrelated frequencies with very brief duration

DURATION Vibrations tend to die out as the energy originally imparted to the system is dissipated in the form of heat from friction If the frictional resistance is increased, the vibratory motion persists for a shorter period of time because it is "damped" (Fig 2*D*) The soft tissues of the body very effectively damp the vibrations of internal structures For example, heart sounds consist of relatively few vibrations, but sounds of longer duration may persist as long as energy is supplied to the vibrating system (murmurs)

The Components of the Heart Sounds

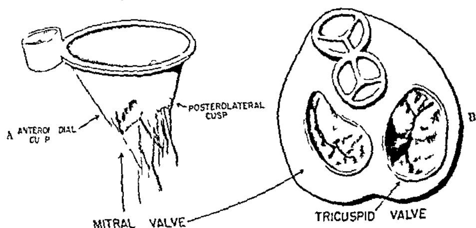
The heart sounds must be considered in relation to the mechanical events of the cardiac cycle The temporal relationships of vibrations produced during the cardiac cycle are most easily established by examining objective records (Fig 3) Many vibrations are inaudible because of their slight intensity For example, low-frequency vibrations associated with atrial contraction can be recorded from the precordium or from the esophagus even though they cannot be heard (Fig 3) The first sound, associated with the beginning of ventricular systole, is frequently divided into four components [1] One or two 'introductory vibrations occur before the ventricular pressures begin to rise (i e , be

against the coronary ostium by a high differential pressure This unfortunate accident is presumably prevented by the presence of adequate space behind the open valve cusps

Atrioventricular Valves

The tricuspid and mitral valves are larger and much more complicated than the semilunar valves The anatomic distinction between the mitral valve and the tricuspid valve

ATRIOVENTRICULAR VALVES



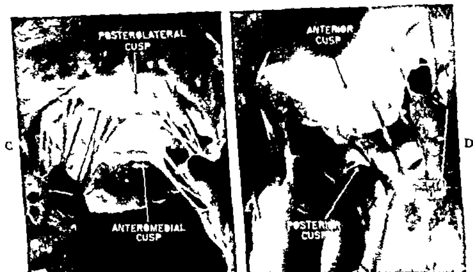


FIGURE 5 *A* The mitral valve is shaped like a funnel when open and is closed by the approximation of two broad, membranous cusps The chordae tendineae originate from the tips of two sets of papillary muscles and prevent eversion of the valve cusps into the left atrium during ventricular systole. The major chordae merge into the edge of the short leaf but may insert several millimeters back from the edge of the larger aortic leaf

B The mitral and tricuspid valves are similar in both structure and function. They both consist primarily of two broad opposing valve cusps with smaller intermediate cusps situated at each end. The tricuspid valve has a somewhat larger intermediate cusp and a total of three separate papillary muscles (After Fig 40 p 391 in Spalteholz, W Hand Atlas of Human Anatomy Philadelphia, J B Lippincott Co 1933)

C In a normal heart specimen, the walls of the left ventricle were excised to illustrate the posterolateral aspect of the mitral valves chordae tendineae and papillary muscles Transillumination reveals that fibers of the chordae tendineae extend long distances within the valve cusps

D The three papillary muscles and corresponding valve cusps of the tricuspid valve were photographed as viewed from within the right ventricular cavity

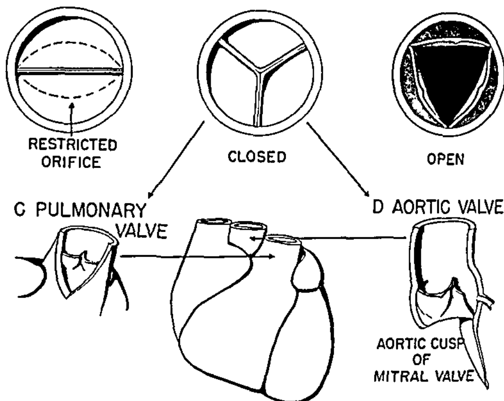


FIGURE 4 *A* Bicuspid valves can close completely but they will not open fully
B A valve with three symmetrical cusps can close completely and theoretically could open to the full dimensions of the artery However motion pictures of aortic valve action have demonstrated that even normal valve cusps are only partly displaced during systolic ejection opening a triangular orifice very much smaller in area than the cross section of the artery (see also Fig 1 Chapter 18) (From McMillan I K R and Daley R The action of human mitral and aortic valves studied postmortem by cinematography presented at the Second World Congress of Cardiology Washington D C. September 16 1954)
C The pulmonary valve is situated at the *junction of the conus region and the pulmonary artery*
D, The aortic valve cusps are in close relation to the orifices of the coronary arteries The sinuses of Valsalva *behind the valve cusps coupled with the incomplete opening of the cusps prevent obstruction of the coronary* orifices during ventricular systole

stitutes are gross caricatures by comparison (see Fig 3, Chapter 18) Not only do they open and close rapidly and seal completely against high pressures with minimal obstruction to flow, but their delicate-appearing cusps may endure the ravages of repetitive closure for more than 100 years

Semilunar Valves

The aortic and pulmonary valves are similar, each consisting of three symmetrical valve cusps Burch and Reaser[14] pointed out the advantages which accrue from this arrangement (Fig 4) Two cusps of equal size *could close tightly, but would not open completely* without considerable elastic stretch *Three cusps can theoretically open* to the full dimensions of the valve ring and yet produce a perfect seal when closed However, recent evidence indicates that normal aortic valves do not open fully (Fig 4*B*, see also Fig 1, Chapter 18) Behind the aortic valve cusps are three outpouchings, the sinuses of Valsalva, which help prevent obstruction of the coronary ostia *If a valve* leaflet came in contact with the coronary orifice, shutting off the flow of blood from the aorta, coronary pressure would fall rapidly as blood left the coronary arterial system, and the valve cusp would be sealed

mm) (see also Chapter 18) Motion pictures[16] show the mitral valve cusps ballooning up into the atrial cavity The chordae tendineae appear to act like clew lines attached to the corners of square sails

The chordae tendineae correspond to multiple guy lines extending from the papillary muscles into the structure of the valve cusps (see Fig 5) It is important to recognize that the chordae tendineae from adjacent regions of the two valve cusps insert upon the same or adjacent papillary muscles (Fig 5) Thus tension exerted through the chordae tends to draw the two valve cusps together If the papillary muscles begin their contraction early in ventricular systole traction on the valve cusps should facilitate apposition of the valves

The Mechanism of Valve Closure

In 1912 Henderson and Johnson[17] reported a series of most ingenious demonstrations of two different mechanisms for closure of heart valves The first mechanism is a retrograde flow of blood toward the atria as *the ventricles begin* to contract catching the valves like a pair of sails and flinging them into apposition (Fig *6A*) Imagine a door being slammed by a gust of wind Clearly this mechanism inevitably involves a large leak before the orifice is closed Such *regurgitation* is widely acknowledged when the atrioventricular valves are closed by ventricular systole which is not preceded by an atrial contraction i e premature ventricular contraction If the mitral valve normally closes *without* regurgitation flow of blood through the mitral orifice during atrial systole *must* bring the valves into partial or complete apposition Henderson and Johnson[17] demonstrated that when flow of fluid through an orifice is suddenly arrested the inertia of the moving blood produces in its wake a negative pressure which closes either simulated or real heart valves (Fig *6B*) The portion of the valves *nearest* their base is the first to move inward and the edges of the flaps are the last to make contact. In this way the valves close without the slightest regurgitation Such inrolling during valve closure 'invariably occurred under conditions simulating the movements of blood in the normal heart

Dean[18] connected the edge of a mitral valve cusp to a delicate lever by means of a human hair and recorded the valve movements in isolated perfused hearts (Fig 7) He found that when the interval between atrial and ventricular systole was less than 0 147 second the valve cusps opened wider at a time when blood was flowing through the orifice and near the end of atrial contraction moved quickly and markedly toward the atrium but not to a position of complete closure The onset of ventricular contraction at this moment completed closure of the valves as a single movement A longer interval between atrial and ventricular systole (greater than 0 27- sec) allowed the valves to move toward apposition and then separate again before ventricular contraction ensued These observations are clearly *consistent* with the concepts of *Henderson* and Johnson[17]

Shearn et al[19] found that the intensity of the *first heart sound* is influenced by the interval between atrial and ventricular systole as indicated by the P R interval Their observations appear consistent with the valve movements *reported* by Dean (Fig 7) The intensity of the first heart sound is related to the position of the heart valves at the onset of ventricular systole the sounds being most intense when the valves are most widely separated The reasons for this relationship will be considered in relation to the mechanisms of heart sound production (*vide infra*)

Cinefluorographic Studies of the Mitral Valve

Direct observations and recordings of functioning heart valves have been rare indeed and all of them have been conducted on exposed or isolated hearts Since the heart in a thoracotomized animal is markedly smaller than normal the valves were probably functioning abnormally during such studies The fibrous valve cusps and chordae

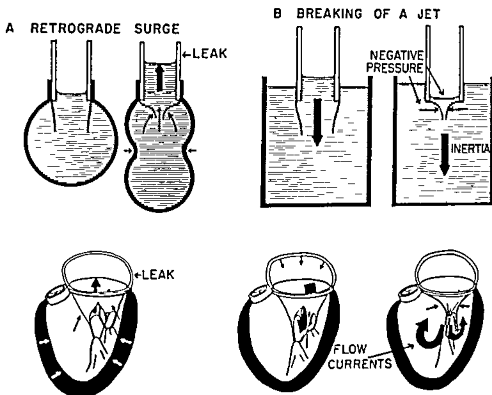


FIGURE 6 Two mechanisms for closure of A V valves are indicated by simple models and by schematic drawings

A A valve consisting of a section of thin walled rubber tubing mounted within a rubber bulb could be closed by a surge of fluid only after considerable leakage past the closing valve Similarly if the mitral valves gape wide at the beginning of ventricular contraction considerable blood would regurgitate into the left atrium during closure of these valves

B If the flow of fluid through a model valve ceases rather abruptly the inertia of the moving fluid carries it onward leaving a wake of negative pressure which could close the valve with no regurgitation whatever Cessation of flow into the ventricle after atrial systole may produce partial closure of the A V valves by this mechanism facilitated by currents of flow upward and behind the closing valve cusps (after Henderson and Johnson[17])

is largely artificial since both valves consist fundamentally of two large opposing cusps and small intermediary cusps at each end However, the chordae tendineae of the tricuspid valve usually insert on three fairly distinct groups of papillary muscles while only two principal papillary muscles serve the mitral valve The anatomy of the papillary muscles is subject to considerable individual variability, some being deeply notched grooved or separated into multiple heads Since the structure and function of the mitral and tricuspid valves are similar, only the former will be described in detail

THE MITRAL VALVE The mitral valve is interposed between the low-pressure left atrium and the high-pressure left ventricle The two valve cusps are unequal in size The large anteromedial (aortic) cusp hangs down like a curtain between the mitral and aortic orifices while the shorter posterolateral cusp originates from the lateral portions of the mitral ring The combined surface area of the two valve cusps is nearly twice as great as the area of the mitral orifice which they must occlude Brock[15] pointed out that the mitral valve orifice is considerably smaller than the mitral ring because the valve cusps are joined at the commissures so the upper portion of the mitral valve resembles a funnel For this reason he believes that the effective mitral orifice at the lower end of the funnel is not significantly greater than the aortic orifice (diameter 26 mm area 530 sq mm) even though the mitral ring is much larger (diameter 32 mm, area 855 sq

tendineae retain their normal size even if the ventricular chambers shrink to very small dimensions so there might be a great deal more slack in the valves of isolated or exposed hearts than in those of normal ones Valve action in intact animals was studied cinefluorographically as indicated in Figure 8

In such experiments the excursion of the valves was surprisingly small Certainly the valve cusps did not gape wide at any phase of the cardiac cycle At no time did the valve edges ascend to the plane described by the mitral valve ring which was marked by silver chains In other words, the valve edges were apparently held well down within the ventricular cavity during all phases of the cardiac cycle To ascertain that large valve excursions were not occurring in some other plane stereoscopic cinefluorographic equipment was developed to study valve motion in three dimensions These studies merely confirmed that the valves moved very small distances

Both the restricted lateral movement during diastole and the limited motion toward the atrium during systole point to more or less continuous restraint by the chordae tendineae The normal traction of the chor-

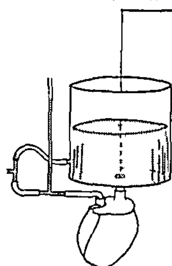
ANATOMY OF THE MITRAL VALVE



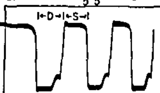
FIGURE 9 On the basis of studies illustrated in Figure 8 these normal human mitral valves are presented in a postulated position of rest with slight tension being exerted by the chordae tendineae From this position slight separation of the valves could admit a rapid flow from the atria or slight movement toward apposition would produce rapid closure with little or no regurgitation

MOVEMENTS OF THE MITRAL VALVE

A APPARATUS FOR RECORDING MOVEMENTS OF MITRAL VALVE



B SHORT A_5V_5 INTERVAL



LEVER

LIGHT BEAM

←HAIR

MITRAL VALVE

C LONG A_5V_5 INTERVAL

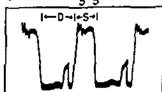
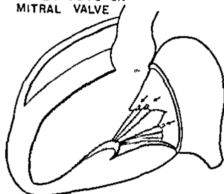


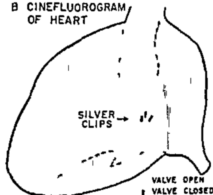
FIGURE 7 Dean's records indicated that during the later part of diastole (*D*) the valve cusps moved toward a position of closure after atrial systole and before ventricular systole (*S*) If the interval between atrial systole and ventricular systole was short valve closure was initiated before ventricular systole and was completed by the rising ventricular pressure If this interval was sufficiently long the valves closed partially and then gaped wide before ventricular contraction ensued (lower record)

MOVEMENTS OF THE MITRAL VALVE IN INTACT DOGS

A SILVER CLIPS ON MITRAL VALVE

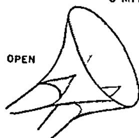


B CINEFLUOROGRAM OF HEART



C MITRAL VALVE ACTION (SCHEMATIC)

VALVE OPEN



VALVE CLOSED

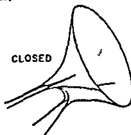


FIGURE 8 *A* Delicate silver chains and silver clips were attached to various points on the valve cusps *B* During and after recovery from the operation the movements of these opaque markers were recorded on cinefluorographic films (exposed at 30 frames per second) and studied by projection and by analysis of successive frames In all experiments the excursions of the metal markers were very limited indicating that the valves of these intact dogs neither separated widely when open nor ballooned up into the left atrial cavity when closed

C, The action of the mitral valves is visualized schematically as being restrained during both diastole and systole by tension on chordae tendineae preventing wide movements of the valve cusps

readily identifiable The character of the vibrations is influenced by the nature of the pecific *cardiohemic system* which is vibrating The term *cardiohemic system* has been coined to cover any combination of blood and heart walls which is the primary site of vibrations produced by changes in velocity of the blood contained therein. The vibrations induced within any cardiohemic system in the heart may be transmitted in all directions and may be audible if they are transmitted to the thoracic walls with sufficient intensity and high enough frequency Using the concept of cardiohemic systems the etiology of heart sounds can be described logically

THE ATRIAL SOUND In the latter part of diastole, the ventricles are well filled with blood and in direct communication with the atria through the partially open atrioventricular valves When atrial contraction displaces blood through these valves the ventricular walls become more distended and stretched as indicated by the slight increase in the intraventricular pressure The recoil of the distended ventricles sets the stage for vibrations back and forth between the atria and ventricles This recoil may also contribute to transient valve closure Since this cardiohemic system consists of the thin-walled right and left atria and relaxed ventricular walls it is not surprising that these vibrations consist of a few low frequency oscillations

THE FIRST HEART SOUND At the onset of ventricular contraction blood is accelerated in the ventricle surging toward the atrioventricular valves This acceleration of blood occurring before the valves are sealed and taut is responsible for the introductory vibrations of the first heart sound (first component) which precede elevation of the intraventricular pressure Their frequency is very low and their intensity is slight presumably because the ventricles remain largely relaxed and the acceleration of blood is not rapid However this movement of blood must be sufficient to close seal and apply tension to the atrioventricular valves before ventricular pressure rises When this movement of the blood is suddenly arrested the valves become tense The second component of the first sound begins as the momentum of the moving blood produces sufficient valvular overstretching to cause a recoil back toward the ventricles (Fig 10 I) In this case, the cardiohemic vibrating systems consist primarily of the two ventricular cavities completely enclosed by valves and contracting myocardium Thus, the vibrations generated at the onset of ventricular systole have a higher frequency and a greater amplitude than those produced by atrial contraction

The intensity of the vibrations depends upon the velocity attained by the blood and the abruptness with which it is decelerated Thus the sound would be greater if the valves gaped wide at the onset of the ventricular contraction than if they were approximated at this moment because the blood would attain a higher velocity before complete closure occurred This concept appears consistent with the observations of Henderson [17] Dean [18] Shearn et al [19] and others [20]

The third component of the first heart sound begins as ventricular contraction elevates the intraventricular pressure above that in the corresponding artery and blood begins to move toward the semilunar valves The inertia of the long columns of blood in the arterial trunks opposes acceleration just as though there were an obstruction a short distance beyond the semilunar valves Therefore the first portion of the blood moving out of the ventricles distends the proximal portions of these arteries Sudden distention of the proximal arterial segments may induce a rebound of blood toward the ventricles Oscillation of the blood back and forth between the arterial roots and the ventricular chambers would result from a mechanism similar to that associated with closure of the atrioventricular valves (Fig 10A) Since the cardiohemic systems producing the second and third components of the first sound are very similar their frequencies intensities and qualities are also similar Indeed these two components are usually merged into a single set of vibrations which cannot be

dae tendineae tends to hold the valves in a position of partial approximation (Fig 9) Under these conditions, the flow of blood through the valve orifice would separate the valve cusps slightly and ventricular contraction would close them promptly with little regurgitation even without a preceding atrial contraction

THE ORIGIN OF HEART SOUNDS

As many as 40 different theories have been proposed to explain the first heart sound [9] Wide divergence of opinion also characterizes the theories regarding the origin of other heart sounds and murmurs This chaotic condition appears to stem from the type of investigation which has been applied to the problem Virtually every possible mechanical event occurring during the cardiac cycle has, at one time or another, been ascribed a role in the production of heart sounds For example, different components of the first sound are attributed variously to vibrations of numerous structures including valves muscular walls and arteries Since the chambers of the heart are filled with blood none of these structures can vibrate independently without producing movements of the blood Similarly, vibrations in the blood must be transmitted to the surrounding structures If the sounds can be picked up from the external surface of the body, all structures between the heart and the thoracic wall must be vibrating It is futile to consider vibrations of the heart walls, valves arterial walls and blood individually when in fact they constitute an interdependent system and all vibrate at the same time A more realistic approach to the problem results from considering those conditions which lead to vibrations of cardiohemic systems composed of the blood, heart walls and valves

Vibrations in Fluid filled Elastic Systems

Vibrations in the cardiovascular system are caused by two general mechanisms (*a*) acceleration or deceleration of blood and (*b*) turbulence developing during rapid blood flow In the subsequent discussion vibrations or sounds due to acceleration or deceleration of blood will be classified as heart sounds Vibrations or sounds due to turbulence in flowing blood will be considered as murmurs (*vide infra*)

In the first portion of this chapter, the characteristics of vibrations were described in terms of a mass supported by a spring (Fig 1) In an elastic chamber completely filled with fluid, the elasticity of the walls is analogous to the spring and the fluid plus the supporting walls is analogous to the vibrating mass Imagine a fluid-filled balloon in which any sudden movement (acceleration or deceleration) throws the entire system into vibration Clearly, no portion of the balloon could vibrate independently without affecting all other portions of the system A sharp tap in a very localized area produces vibrations affecting all parts of the fluid and the walls The vibrations are due to the momentum of the fluid producing an overstretch of the elastic wall which recoils and displaces the fluid in the opposite direction This sequence is repeated until the residual energy in the system is dissipated The intensity of the vibrations is determined largely by the rate of change of velocity (the amount of acceleration or deceleration) Their frequency depends upon the relation between the vibrating mass and the elasticity of the walls In the heart, the combined mass of the blood and the walls of the chambers is very large in relation to the elasticity of the walls, so the vibrations usually have a low frequency When the ventricles are contracting, the elasticity of the walls should be greater and the vibration frequency increased Vibrations due to acceleration and deceleration of blood tend to consist of only a few cycles indicating that they are promptly damped

Cardiohemic Systems in Heart Sound Production

From a knowledge of the mechanical events of the cardiac cycle, the regions where acceleration or deceleration of blood is occurring at any particular phase should be

readily identifiable The character of the vibrations is influenced by the nature of the specific *cardiohemic system* which is vibrating The term *cardiohemic system* has been coined to cover any combination of blood and heart walls which is the primary site of vibrations produced by changes in velocity of the blood contained therein The vibrations induced within any cardiohemic system in the heart may be transmitted in all directions and may be audible if they are transmitted to the thoracic walls with sufficient intensity and high enough frequency Using the concept of cardiohemic systems the etiology of heart sounds can be described logically

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THE ETIOLOGY OF HEART SOUNDS

A COMPONENTS OF FIRST HEART SOUND

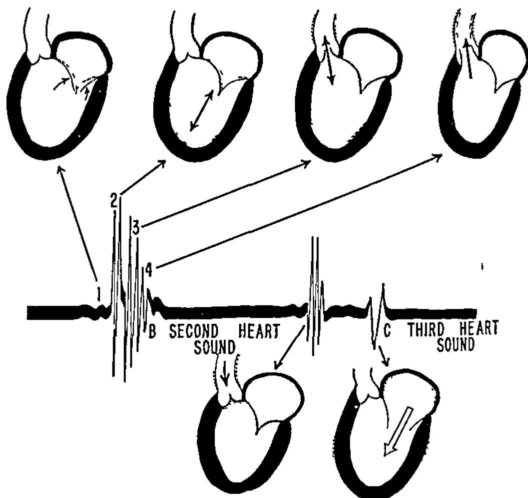


FIGURE 10 Causes of various components of the heart sounds are presented in schematic drawings based on the concept that the vibrations are induced by acceleration or deceleration of the blood within elastic chambers

A The first sound can be divided into four components (see Fig 3) The initial vibrations occur when the first myocardial contractions in the ventricle shift blood toward the atrium to approximate and seal the atrioventricular valves The second component begins with abrupt tension of closed atrioventricular valves decelerating the moving blood (Fig 3) It may represent oscillation of blood initiated by overdistention of the atrioventricular valves countered by recoil of the contracting ventricular myocardium The reaction would be similar to tapping a balloon filled with water The third component may involve oscillations of blood between the distending root of the aorta and the ventricular walls The fourth component probably represents vibrations due to turbulence in blood flowing rapidly through the ascending aorta and pulmonary artery (see also Fig 16)

B The second heart sound is introduced by a few low frequency vibrations which may accompany the deceleration and reversal of flow through the aorta and pulmonary artery prior to the closure of the semilunar valves The audible portion of the second sound begins with closure and tensing of the semilunar valves Although the primary vibrations occur in the arteries they are also transmitted to the ventricles and atria by movements of the blood valves and valve rings

C The third heart sound occurs at the end of the rapid filling phase Sudden termination of the rapid filling phase may throw the entire atrioventricular system into vibrations which have very low frequency because the walls are relaxed

differentiated Splitting or reduplication of the first sound might be attributed to temporal dissociation or cancellation of the vibration set up by abrupt closure of the atrioventricular valves and the vibrations due to abrupt arterial distention

The fourth component of the first heart sound is probably the result of turbulence in the blood flowing rapidly through the arterial trunks and for this reason will be considered under murmurs (*vide infra*)

THE SECOND HEART SOUND Near the end of systole the rate of ejection slows as the ventricular and arterial pressures begin to diminish Ventricular pressure drops precipitously at the onset of ventricular relaxation Blood in the roots of the aorta and in the pulmonary artery rushes back toward the ventricular chambers but this movement is abruptly arrested by closure of the semilunar valves The momentum of the moving blood overstretches the valve cusps and the recoil initiates oscillations in both the arterial and the ventricular cavities (Fig 10*B*) The pitch of the second sound seems higher than that of the first sound The intensity of the sound again depends upon the velocity attained by the blood gushing back toward the ventricle and the abruptness with which the motion is arrested In systemic or pulmonary hypertension the velocity should be great and the sounds intensified In the presence of semilunar valvular stenosis on the contrary the amplitude of the second sound should be reduced if the valves are largely approximated before the retrograde flow is well established

THE THIRD HEART SOUND When intraventricular pressure drops below atrial pressure the atrioventricular valves swing open before a mass movement of blood into the relaxed ventricular chambers Inflow is arrested rather suddenly as is manifested by the rapid transition from the rapid filling phase to the plateau which indicates slow filling or diastasis The momentum of the moving mass of blood produces low frequency vibrations because the chamber walls are all relaxed Such vibrations would be more likely to occur when the rapid filling phase terminates abruptly Because of their low frequency, the vibrations must have considerable amplitude to reach the auditory threshold, particularly if the loss of energy during transmission is great Third heart sounds are more frequently heard in children with thin chests

GALLOP RHYTHMS When three audible heart sounds occur in rapid succession followed by a pause the subjective impression is similar to the sounds produced by a galloping horse Several combinations of heart sounds can produce this impression The most common form of gallop occurs when the third heart sound is clearly audible In this case the three heart sounds occur in sequence and are followed by a relatively silent interval during the remainder of diastole This type is frequently called the *protodiastolic* gallop which is a misnomer because the third sound follows the protodiastolic interval For no very good reason third heart sounds commonly heard in normal children are usually not included among gallop rhythms A gallop rhythm which develops in the course of heart disease (e g myocarditis congestive failure) signifies alterations in the myocardium The third heart sound is so rarely audible in aged individuals that the protodiastolic gallop often indicates a serious prognosis The nature of the myocardial change which accentuates the third heart sound is not clear, but presumably the rapid filling phase is terminated more abruptly

If the sounds accompanying atrial systole are intensified and precede the first sound by a sufficient interval to be distinguished a gallop rhythm is produced which consists of the fourth, first and second heart sounds in succession Since the abnormal sound occurs in late diastole this rhythm is called a presystolic gallop

If the heart rate is rapid the diastolic interval becomes shorter and the third and fourth heart sounds may occur almost simultaneously The combined intensity of the two sets of vibrations may become audible

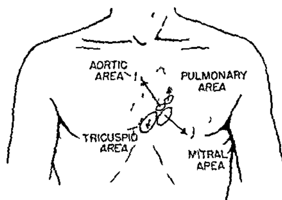


FIGURE 11 Although heart sounds are widely transmitted over the precordium vibrations from the four valves tend to be transmitted with maximal intensity to areas on the precordium as indicated by the arrows above The mitral area on the precordium is near the apex of the heart the tricuspid area is in the fourth intercostal space on either side of the sternum The pulmonary area is in either the second or the third intercostal space at the left parasternal line, and the aortic area is in the second right intercostal space but often extends obliquely across the precordium toward the apex (see Fig 17)

and the resulting rhythm is called a *summation* or mid-diastolic gallop

Transmission of Sounds

The factors that influence the transmission of vibrations are the same as those involved in their production (see Fig 2) The elasticity or restoring force of the transmitting media is very important Since the mass of vibrating material (the heart, blood and tissues) is great in relation to tissue elasticity, low-frequency sounds predominate in both production and transmission This is most unfortunate because the human auditory mechanism is particularly insensitive to low-pitched sounds (see *Auditory Perception of Heart Sounds*, below)

Since the heart sounds are composed of vibrations with long wave lengths (low pitch) their transmission from the point of origin to the surface of the body differs materially from that of the waves illustrated in Figure 1 To produce four vibration cycles traveling at a rate of 1100 ft per second within a length of tube 1 ft long the tuning fork must vibrate at about 4400 c p s If the tuning fork oscillates at a rate of only 100 c p s, the cycle length is 11 ft, longer than the transmission distance through the tube Under these conditions, the air in the tube would be alternately compressed and rarefied

Vibrations in the heart are probably transmitted to the surface of the skin at the velocity of sound transmission through water (almost 5000 ft per second) The maximum transmission distance from the heart to the surface of the chest is less than a foot, and the cycle length of the vibrations is greater than this distance For this reason, all the structures involved in the transmission of these vibrations to the surface tend to oscillate back and forth together Under these conditions, sound waves are not reflected The most important loss of heart sound energy occurs in compressible tissues (e g lung) interposed between the heart and chest wall Vibrations of the heart wall may be so well damped while passing through a thick cushion of aerated lung tissue that they are poorly transmitted to the chest wall (e g emphysema) Thus, the heart sounds have maximum intensity in those surface areas to which the vibrations are transmitted directly through solid tissues or through a minimal thickness of inflated lung Layers of fat also attenuate heart sounds because of damping

SURFACE LOCALIZATION OF HEART SOUNDS Sounds emitted from the vicinities of the four valves have maximal intensities at four different surface areas For example murmurs from the region of the pulmonary valve are most intense in the *pulmonary area* centered at the third left intercostal space at the left parasternal line (Fig 11) The *aortic area* lies to the right of the sternum in the second right intercostal space The *tricuspid area* is near the right sternal border in the fourth intercostal space and the *mitral area* is near the apex of the heart This particular localization of sounds on the surface probably represents the most effective transmission pathways from the original sites of vibration to the surface of the chest The pulmonary and tricuspid valves are near the precordium and the corresponding ausculta

tory areas are close by The aortic and mitral valves are situated farther from the precordium and their auscultatory areas do not overlie the valve rings (Fig 11) In the region of the apex, the heart sounds are usually loud because the heart is in direct contact with the anterior wall of the thorax Vibrations of the ventricular chamber associated with mitral valvular disease are frequently localized over the apex The ascending aorta curves forward and most closely approaches the anterior chest wall near the aortic area Sounds emitted from the region of the aortic valve may also traverse the right ventricular chamber to appear in the third or fourth intercostal space to the left of the sternum or follow the left ventricular chamber to a point near the apex

The fact that both the first and second heart sounds are generally audible at all four areas indicates that their production is not limited to vibrations in the regions of the valves The wide distribution is consistent with oscillation of cardiohemic systems produced by mass movements of blood

It is inaccurate to consider the second sound in the pulmonary area to be composed primarily or exclusively of vibrations from the pulmonary valve In records taken from directly over the valve rings on the surface of the heart the contribution of one valve cannot be dissociated from that of another The reason for this becomes apparent when it is recognized that the atria ventricles arterial trunks and valves are all firmly fastened to the fibrous skeleton of the heart (Fig 1 Chapter 1) and must all be affected by vibrations at any point Nevertheless a loud second sound in the pulmonary area on the precordium is frequently a reliable indication of pulmonary hypertension and its localization permits its differentiation from a loud aortic second sound which may occur with systemic hypertension

Auditory Perception of Heart Sounds

Under optimal conditions the ear can detect vibrations with an amplitude less than the diameter of a molecule The energy of barely perceptible sound waves is so slight that it would have to be continued without loss or interruption for more than two million years to elevate the temperature of 1 gm of water 1° C.[4]

Although the maximal range of audible frequencies normally lies between 20 and 16 000 c p s the maximal sensitivity of human audition lies within the speech range about 1000 to 2000 c p s[25] To be perceived sound with a frequency of 30 c p s must attain energy levels thousands of times those needed by vibrations at 1000 c p s (Fig 12) Heart sounds extend above and below the threshold of hearing so some are inaudible while others considerably exceed threshold levels The frequencies of the audible vibrations of the heart probably range from below 20 c p s to above 200 c p s (The frequencies of murmurs may be as high as 600 to 1000 c p s.) Owing to extreme lack of sensitivity to low frequency vibrations, the auditory mechanism may perceive relatively weak overtones of heart sounds more clearly than the more intense low frequency fundamental vibrations[26] Thus the low frequency vibra

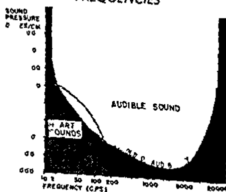


FIGURE 12 The threshold of audibility varies for different sound frequencies The auditory mechanism is far more sensitive to frequencies in the speech range (1000 to 2000 c p s) than to sounds of either higher or lower pitch. The heart sounds are primarily low frequency vibrations Only a portion of the vibrations have sufficient intensity to reach the auditory threshold the remainder being completely inaudible. Certain of the high-pitched murmurs reach frequencies of 1000 c p s and can be perceived even when the sound energy is relatively slight.

tions, which are most easily recorded electronically, may constitute only a portion of the heart sounds which are heard during auscultation

When listening to sounds of a particular frequency, the human hearing apparatus speronds to sounds of very low and very high energy At certain frequencies the energy level of the threshold for pain is more than three million times that for the threshold of audibility This tremendous range of perceptible intensity is possible because the perceived "loudness" is proportional to the logarithm of the stimulus strength In other words, if the sound intensity is doubled successively, the "loudness' of the sensation increases in equal steps (see Fig 13C) Thus, the auditory mechanism can respond to a tremendous range of sound energies while retaining sensitivity to sounds of very low intensity

In complex sounds, the low-pitched tones often seem more prominent because the higher pitched tones become masked This phenomenon is more marked when the intensity of the low tones is increased Thus, the quality of sounds may be affected by any factor which alters the intensity The higher frequencies found in diastolic murmurs can often be brought out by judicious use of the stethoscope selectively attenuating the low frequencies

STETHOSCOPES Heart sounds can be readily heard by placing the ear directly on the chest of the patient Stethoscopes are employed for the sake of convenience and propriety rather than to amplify the sound Sounds are both damped and distorted by stethoscopes When an open bell is applied to the chest the skin forms a diaphragm while the underlying tissues act as a damping medium [27] If the bell is held firmly against the skin, the low frequencies are attenuated more than the higher frequencies, which seem louder even though their actual sound energy is diminished A similar effect can be produced by using a Bowles type stethoscope with a plastic diaphragm covering the air chamber In any case, the presence of a taut diaphragm produces attenuation of the low frequencies which is useful in detecting the high-pitched diastolic murmurs, but undesirable in eliciting faint, low-pitched murmurs A most complete analysis of the factors in the auditory perception of heart sounds and murmurs was presented by Rappaport and Sprague [27] Included in their investigation was the influence of various types of stethoscopes on auscultation For example, it is not generally recognized that properly fitting ear pieces on stethoscopes are extremely important since a leak with a diameter approximately five times that of a human hair may markedly reduce perception of heart sounds and murmurs [28]

Lepeschkin[29] recently devised a most ingenious quantitative stethoscope with an adjustable orifice in the chest piece so that sound intensity may be graded far more accurately than by purely subjective impression

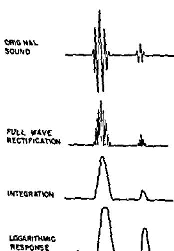
PHONOCARDIOGRAPHY Verbal descriptions of sounds (e g , harsh, coarse, ringing, etc) are notoriously inadequate For this reason, phonocardiography affords a common meeting ground for the discussion of heart sounds The temporal relations between the heart sounds and mechanical events of the cardiac cycle are of paramount importance in interpreting the significance of sounds and murmurs In this sphere, phonocardiography makes its greatest contribution

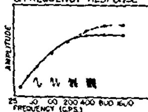
The heart sounds are so attenuated and modified by transmission through various media and by the vagaries of auditory perception that it is manifestly impossible to produce heart sound records which match the sounds heard during auscultation Rappaport and Sprague[27] have discussed in detail the essential characteristics of heart sound recording equipment In subsequent sections heart sounds and murmurs will be illustrated by two types of records (a) standard phonocardiograms from instruments using high frequency amplifiers and galvanometers and (b) simplified heart sound recordings which indicate only sound intensity (sonvelograms)

SONVELOGRAPHY A device for recording heart sounds and murmurs as an envelope of the sound intensity was developed in the author's laboratory[30] and has been called the sonvelograph (*son* = sound, *velo* = to envelope). The derivation of sonvelograms from the heart sound vibrations is illustrated in Figure 13. The resulting records indicate timing and relative intensity of sounds during the various phases of the cardiac cycle. The amplifier has characteristics similar to those of the human auditory apparatus (Fig 13*B*) so the records resemble the simple sketches that clinicians frequently draw to indicate the presence and timing of murmurs. Being designed for use with standard direct writing electrocardiographic equipment, the envelope of sound is a reliable indication of the logarithm of sound intensity regardless of frequency. Although sonvelograms are not suited for research on heart sounds, they are useful in clinical diagnosis and as illustrations because their interpretation is so simple. Sonvelographic records of the heart sounds and various types of murmurs are illustrated in Figure 14.

HEART MURMURS

In the preceding discussion, the etiology of heart sounds has been ascribed to vibrations induced by sudden displacement of blood (acceleration) or by abrupt cessation of flow (deceleration). In contrast, heart murmurs are defined here as the result of turbulence developing in rapidly flowing blood. These definitions provide clear functional and physical distinctions between the heart sounds and murmurs. Since causes of





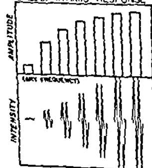


FIGURE 13 Sonvelograms are continuous recordings of an envelope of the heart sound intensity.

A. Sound waves are converted into fluctuations in voltage by an appropriate microphone. These fluctuating voltages can be amplified and recorded directly as phonocardiograms (see Figs 3 and 10). Sonvelograms are derived by full-wave rectification of these signals so that all deflections have the same polarity. The time constant of the amplifier is adjusted so that the record corresponds to a line connecting the peaks of these deflections.

B. The frequency response of the sonvelographic amplifiers resembles that of human auditory perception, having low sensitivity to low frequencies (see Fig 12).

C. The amplifier has a logarithmic response to vibrations of different intensity similar to that of the human ear. The logarithmic response tends to accentuate sounds of low intensity as indicated by the bottom schematic record on the left.

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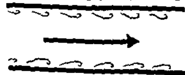
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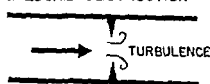
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lined flow (Fig 4 Chapter 2) The conditions producing turbulence in fluid flowing through tubes of constant caliber are expressed in the formula RVD/v = critical constant for turbulence (Reynolds number)[31] where fluid of viscosity v and density D flows with a mean velocity V through a tube of radius R This formula indicates that turbulence occurs when fluids of low viscosity flow at high velocity through tubes of large diameter (Fig 15*A*) Since the blood viscosity and the vascular diameter are relatively constant the *major* variable is the velocity of blood flow The critical level of Reynolds number for turbulence in blood is reported as 970 ± 80[3] Blood flows rapidly through the largest arterial channels and at the highest velocity in the roots of the aorta and the pulmonary artery According to Prec et al [33] the critical level for turbulence is normally exceeded at these sites during the rapid ejection phase of ventricular systole On this basis the vibrations usually classified as the fourth component of the first heart sound are probably due to turbulence and are actually an early systolic murmur according to the definitions being used here On this basis virtually all individuals have an early systolic murmur even though its duration is insufficient for its detection (see *Functional Murmurs* below)

Turbulence tends to occur where the caliber of a channel enlarges abruptly For example, when fluid must flow through a restricted orifice, eddy currents are prone to develop just beyond the obstruction (Fig 15*B*) In such circumstances turbulence will occur when the flow velocity is much smaller than in a tube of constant bore Similarly when a narrow channel opens into a large cavity turbulence is likely to develop at relatively low flow velocity (Fig 15*C*) When the two factors in *B* and *C* are combined the tendency toward developing turbulence is greatly increased (Fig 15*D*) Flow in either direction through such a restricted orifice will cause turbulence This is the basic mechanism for the develop-

CAUSES OF TURBULENCE







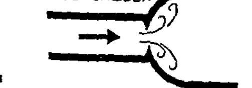


FIGURE 15 Laminar flow of fluids through tubes is silent, but turbulent flow produces vibrations

A Turbulence tends to occur in fluids of low viscosity flowing at high velocity through tubes of large caliber in accordance with the formula for Reynolds number (see text)

B In a tube of uniform caliber inserting a local obstruction produces turbulence at much less velocity of flow

C Turbulence also tends to occur at reduced velocity where fluid flows into a channel of much larger diameter

D When an obstruction occurs at the junction between a narrow channel and a wide one relatively low velocity flow produces turbulence because the factors illustrated in *B* and *C* exert a combined effect.

SONVELOGRAPHIC RECORDS OF HEART SOUNDS AND MURMURS

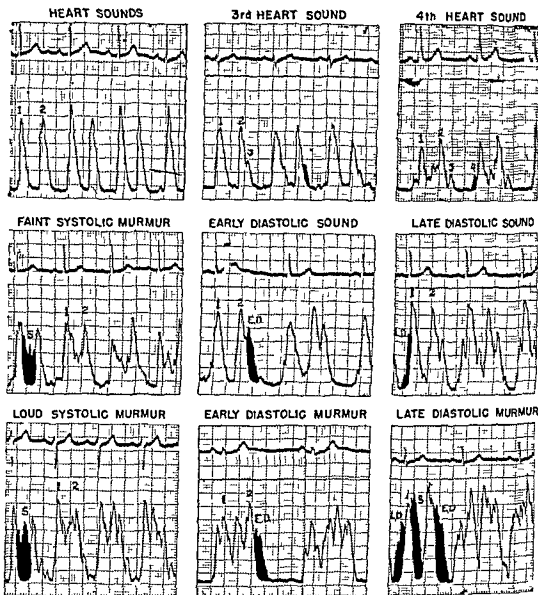


FIGURE 14 Sonvelographic records consisting solely of deflections from the first and second heart sounds (upper left) are the most common type obtained from normal adults Deflections representing first second third and fourth heart sounds are illustrated (upper right) Systolic murmurs are indicated in the column at the left (black areas) Early diastolic murmurs are presented in the middle column and look like intensification and prolongation of the third heart sound Late diastolic (presystolic) murmurs occur just before the first sound and resemble greatly exaggerated fourth heart sounds A record revealing a systolic murmur and early and late diastolic murmurs in a patient with rheumatic valvular heart disease is illustrated in the lower right hand corner

turbulence are well known, the etiology of most murmurs should be explained simply and logically The pathologic conditions which predispose toward such turbulence are well established in most cases Certain types of murmurs have no satisfactory explanation at present, which simply means that we lack essential information concerning conditions in the heart producing these vibrations

Causes of Turbulence in Flowing Blood

The flow of blood through virtually all vascular channels of the body is silent be cause the fluid exhibits laminar or stream

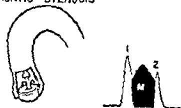
subject leans forward and holds his breath after a forced exhalation. In patients with anemia hemic murmurs develop because the viscosity of the blood is diminished while the flow velocity is accelerated owing to an increase in cardiac output.

Systolic Murmurs Due to Valvular Abnormality

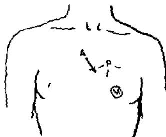
Detection and recognition of heart murmurs is a valuable source of information concerning the function of heart valves. Although the mechanisms producing these sounds are very similar, certain types of valvular disease produce typical sound patterns which can be distinguished on the basis of frequency, transmission and timing.

AORTIC STENOSIS. The aortic valve lies at a considerable distance from the precordium. Vibrations from this source reach the precordium after transmission directly from the ascending aorta (aortic area), through the pulmonary artery and conus (third left intercostal space), or through the ventricles toward the apex of the heart. Systolic murmurs of aortic origin have been clearly demonstrated in the broad area indicated in Figure 17C. Thus aortic murmurs may be localized at various points on the precordium along a line paralleling the outflow tract of the left ventricle. Systolic murmurs of early aortic stenosis may be evidenced only in the pulmonary area and may be difficult to differentiate from functional murmurs. Levine[34] emphasized the fact that these murmurs tend to have maximum intensity in the mid-systolic period and used this criterion to differentiate such murmurs from func-

SYSTOLIC MURMURS FROM VALVULAR DEFORMITY







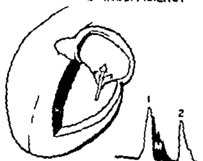


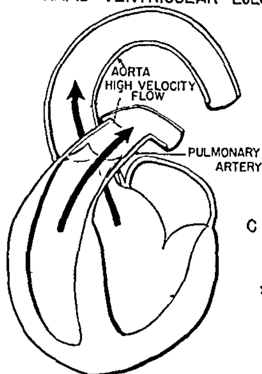
FIGURE 1 A. Aortic stenosis produces a membranous obstruction with a small orifice through which blood is ejected at high velocity during systole. The resulting systolic murmur tends to reach maximum intensity in mid-systole and is usually transmitted primarily to the aortic area. In different patients the region of maximal intensity may occur anywhere in an area extending from the second left intercostal space toward the apex of the heart.

B. Pulmonary stenosis produces a loud systolic murmur extending through the systolic interval, although the intensity is often greatest immediately after the first sound and diminishes progressively. The murmur is transmitted widely over the entire precordium.

C. The surface localization of systolic murmurs originating from various valves is indicated schematically (see also Fig. 11).

D. Mitral insufficiency produces systolic murmurs with maximum intensity near the apex of the heart.

FUNCTIONAL SYSTOLIC MURMURS



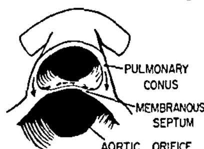




FIGURE 16 *A* Under normal conditions blood flows through the aorta and pulmonary arteries at sufficient velocity to produce turbulence during the rapid ejection phase of ventricular systole Early systolic murmurs can be heard in many normal children at rest and in virtually any normal subject after exercise.

B The right ventricular outflow tract has a roughly crescentic cross-sectional area due in part to the fact that the membranous portion of the interventricular septum bulges into the lumen Bundles of myocardial fibers encircling the conus region tend to further diminish the cross-sectional area of this channel during systole For these reasons turbulence is more likely to develop in the pulmonary artery than in the aorta Systolic murmurs in normal subjects usually have maximal intensity in the pulmonary area on the precordium.

C An early systolic functional murmur may be regarded as an intensified fourth component of the first heart sound (see Figs 3 and 10)

ment of murmurs due to organic valvular heart disease

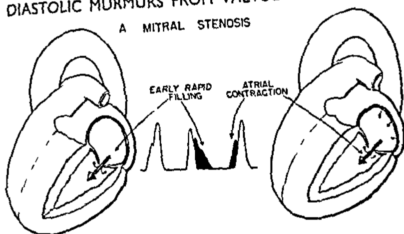
On the basis of this description, additional points of distinction between heart sounds and murmurs can be drawn Turbulence can develop in rather restricted areas, and for this reason, murmurs may be localized to relatively small areas on the precordium Because of basic differences in etiology, murmurs usually have longer duration, higher frequency and more discrete localization than heart sounds

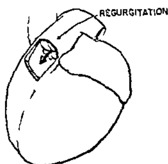
Functional Murmurs

Vibrations during the early ejection phase of ventricular systole can be recorded in virtually all individuals, even though murmurs cannot always be heard (Fig 16*A*) Early systolic murmurs can be heard in a large proportion of children particularly those with thin chest walls In these individuals, all the heart sounds are loud because so little energy is lost in transmission to the surface Such murmurs are classified as functional and are most commonly heard at the pulmonary area on the precordium Although the velocity of flow through both the pulmonary artery and the aorta is sufficient to produce turbulence in early systole certain additional factors present in the outflow tract of the right ventricle are generally overlooked (Fig 16)

Audible early systolic murmurs are usually produced by the increased velocity of flow in almost all normal individuals following vigorous exercise particularly if the

DIASTOLIC MURMURS FROM VALVULAR DEFORMITY





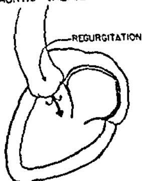


FIGURE 18 A Mitral stenosis produces murmurs occurring primarily during rapid flow through the mitral valve during rapid ventricular filling in early diastole and during atrial systole The murmur has a very low frequency and may be difficult to hear even though the sound intensity is great The early diastolic murmurs tend to be localized fairly discretely at the apex of the heart.

B Pulmonary insufficiency permits regurgitation of blood into the right ventricle during diastole The resulting murmur tends to have maximum intensity in the pulmonary area but is often transmitted over a wide area on the precordium

C Aortic insufficiency tends to produce high-pitched diastolic murmurs usually heard best in the aortic area but occasionally most intense in the pulmonary area or even near the apex of the heart

mur becomes audible in the pulmonary area

Pulmonary valvular insufficiency permits the regurgitation of blood during the diastolic interval which accounts for the diastolic murmur The regurgitant stream flows rapidly through slits between the valve cusps and enters a large ventricular chamber (see Fig 18*B*)

AORTIC INSUFFICIENCY Aortic insufficiency without stenosis generally results from cardiovascular syphilis (Fig 18C see also Fig 1 Chapter 18) Systolic murmurs generally accompany the diastolic murmur because the regurgitation increases the rate and volume of ventricular ejection Combined systolic and diastolic murmurs resemble the sounds produced by sawing wood with a hand saw, the systolic murmur representing the cutting stroke and the higher pitched diastolic murmur corresponding to the back stroke

The Significance of Palpable Thrills

Vibrations produced by murmurs occasionally have such great intensity that they may be palpated on the surface of the chest In comparison to auditory perception, the tactile vibratory sense is extremely insensi

tional, pulmonary or mitral systolic murmurs

PULMONARY STENOSIS Uncomplicated pulmonary stenosis, either congenital or acquired, is relatively rare Fusion of the pulmonary leaflets produces a local constriction beyond which turbulence occurs during systolic ejection from the right ventricle (Fig 17*B*) The resultant loud, harsh, systolic murmur usually has maximum intensity in early systole, the intensity diminishing during the systolic period. Such murmurs are heard most loudly in the pulmonary area (see also Fig 11, Chapter 18) and are widely transmitted over the precordium Pulmonary stenosis is usually due to a congenital malformation

MITRAL INSUFFICIENCY If for any reason the mitral valve cusps fail to completely occlude the mitral orifice, blood rushes through the defect during ventricular systole, propelled by the large pressure difference between the left ventricles and left atrium The gap between the valve cusps acts as a local constriction through which the blood squirts at high velocity into the capacious atrial chamber (Fig 17*D*) The resulting turbulence produces an apical systolic murmur which is ordinarily widely transmitted, particularly toward the left axillary region

Diastolic Murmurs Due to Valvular Abnormality

MITRAL STENOSIS The blood flows rapidly from the atria into the ventricles during the early filling period and during atrial systole The fact that the diastolic period is normally quiet indicates that the velocity of flow is insufficient to induce significant turbulence and that the mitral and tricuspid orifices do not constitute a local constriction Thus, diastolic murmurs are rarely encountered unless there is some form of organic disease

Rheumatic valvulitis may convert the efficient, flexible mitral valves into a rigid funnel with a narrow elliptical orifice (see Fig 6, Chapter 18) This local constriction between large chambers satisfies all the requirements for the production of turbulence if blood flow attains sufficient velocity (Fig 18*A*) The sequence of events leading to advanced stenosis will be discussed in Chapter 18 A low frequency murmur which immediately precedes the first sound is the classical finding in mitral stenosis In the early stages, this presystolic murmur can be easily missed since it is often localized to a very small area at or near the apical region on the precordium The murmur may be audible only when the patient reclines in the left lateral position or after exertion The low-pitched "rumble" seems to gather intensity and terminate in an accentuated first sound Since this murmur frequently disappears in patients who develop atrial fibrillation, its presence has been attributed to rapid flow through the stenosed valve during atrial contraction

In many cases of mitral stenosis, an early diastolic murmur predominates. This murmur occurs during the phase of rapid ventricular filling and attains maximum intensity shortly after the second sound Thereafter, the murmur usually diminishes in intensity, frequently disappearing during the mid diastolic period (see also Fig 9 Chapter 18)

In many patients, the murmur appears to develop maximum intensity in mid-diastole This is probably due to two factors (*a*) A very slight interval between the second sound and the initial vibrations of the murmur gives a mistaken impression that the peak intensity occurs later than is revealed on heart sound records (*b*) In some patients the rapid filling period may be prolonged because of the resistance offered by the restricted orifice The vibrations have such low frequency that they frequently escape detection even when the recorded deflections appear large on phonocardiograms

PULMONARY INSUFFICIENCY Dilatation of the pulmonary artery due to sustained pulmonary hypertension may render the pulmonary valves insufficient When the pulmonary valves fail to approximate a diastolic mur-

stethoscope is placed near the apex the timing of the first sound can be correlated with the precordial thrust When the identity of the first sound is definitely established attention should be confined to this sound alone during several successive cycles If the listener voluntarily blanks out all other sounds in the cycle the first sound can be subjectively isolated Several characteristics of the first sound should be noted individually and in sequence including intensity duration relative frequency or pitch, splitting etc The loudness of the sound must be interpreted in light of judgment concerning the transmission characteristics and hemodynamic situation of the individual subject For example a loud first sound in an obese subject has far greater significance than one of a similar intensity in an asthenic adult or a thin-chested youth The intensity of the vibrations is also affected by the vigor of ventricular contraction heart rate cardiac output P R interval and similar factors The relative intensity of the first and second sounds provides an additional clue concerning these factors

The next step is to direct attention solely to the second sound for a period sufficient to establish its characteristics The loudness of the first sound and second sound can then be compared, but a final decision concerning this observation should be deferred until other areas of the precordium have been examined At this stage *the first and second sounds at the apex should be so familiar that they can be recognized without reference to the apex beat*

A systematic search for murmurs is initiated by directing attention solely *to the interval* which follows each first sound Little experience is required to focus on this interval without actually hearing the first sound Listening first for low pitched sounds and then for high-pitched sounds is a good policy because attention is so discrete that involuntary anticipation of low frequency vibrations may cause one to overlook a high-pitched murmur Having ascertained that the early systolic interval is either quiet or occupied by a murmur attention is next directed toward the later portions of systole If a murmur is present during either of these portions of systole the attention can then be spread to include the whole of the systolic interval to determine the time at which the murmur reaches maximum intensity This technique is the best way to differentiate early systolic murmurs from mid-systolic and late systolic murmurs

The diastolic interval is scanned in the same way Attention is directed first to the interval immediately following the second sound Focussing the attention on the early diastolic interval during a succession of beats is extremely important because it provides the only hope of detecting third heart sounds or early diastolic gallop the opening snap of mitral stenosis and certain early diastolic murmurs It is even more important to listen for both low-pitched and high pitched sounds *during this interval*

The period just *preceding the first sound* is then selectively analyzed For many individuals this is the most difficult step of all because there is no specific stimulus for turning on the attention during each cycle If the heart is beating regularly this difficulty can be easily overcome because the rhythm is established With practice the presystolic interval can be scanned even in the presence of arrhythmia Similarly the process of directing selective attention to a particular interval while voluntarily blanking out all others is more difficult during tachycardia This technique is not only applicable but *absolutely* essential when the heart is beating rapidly or irregularly

When a detailed analysis of the heart sounds and murmurs at the apex has been *completed* the same process is repeated in the pulmonary the aortic and the tricuspid *areas If a* murmur is recognized in any of the intervals the region of maximum intensity and the extent of transmission should be established By limiting attention only to the murmur in question these characteristics can be determined very quickly by *systematically* listening over a sequence of points

tive The palpation of a thrill indicates the great intensity of the vibrations, but provides no information of diagnostic significance that is not gained by auscultation [35]

Variability in Detection of Heart Murmurs

Whenever a group of physicians gather beside a patient with cardiac disease, differences of opinion concerning the auscultatory findings almost invariably arise Such controversies result from differences in auditory acuity, training, and the technique of listening complicated by extreme difficulty in describing auditory sensations The drawing of sketches indicating the intensity and timing of murmurs makes it possible to compare the impressions of different examiners (see Fig 3, Chapter 20) When examiners are confronted with patients with advanced heart disease, the differences of opinion are lessened, but are by no means eliminated Recognition of the limitations of auscultation is the first step toward its maximal effective use as a diagnostic tool The most common deficiency is the inability to perceive certain low-frequency sounds For example, many examiners consistently miss third heart sounds or low-frequency diastolic murmurs Timing of murmurs by auscultation also presents problems to some clinicians Although some of the difficulties may result from depressed auditory acuity, an improper approach to auscultation is frequently the source of the trouble

A SYSTEMATIC APPROACH TO AUSCULTATION

The body is continuously bombarded by sensory stimuli of all kinds, but their entry into consciousness must be restricted to one at a time to make any order out of chaos It is impossible to listen attentively and still be acutely aware of visual images odors proprioceptive stimuli or pain If an attempt is made to concentrate on two things simultaneously, attention rapidly shifts from one to the other with little detailed information being gained from either source Thus, the ability to concentrate on a single source of *stimuli is an essential* characteristic of human perception Similarly, innumerable complex sound waves impinge continuously upon the ear, but most of these sounds *fail to reach* conciousness While you read these words, you are probably ignoring the sounds in your immediate environment

However, undivided attention is insufficient for accurate auscultation If an examiner listens to all the noises emitted by the heart, his attention is usually directed toward the most intense sounds, which may not be the most meaningful It is necessary to utilize a high degree of "selective" attention to gain the maximum information from auscultation Consider how many common sounds can be identified as coming from a specific source such as a nearby radio, a familiar voice, the sound of a car, the creak of a chair, or footsteps Some of these vibrations are sustained, others are intermittent and still others may occur singly, but if they are familiar, their source can be immediately recognized The ability to synthesize combinations of complex sound waves and overtones into patterns which can be identified represents an important attribute of audition As an example, a symphony orchestra emits sound waves having a wide range of frequencies of almost inconceivable complexity One can listen to the music as a harmonic entity made up of sounds from all the instruments On the other hand, the sounds produced by a single instrument may be extracted from this mass of complex sound waves by merely directing attention toward them The conductor is constantly alert to tones which are off beat or out of tune He can instantly fix the offender with a malevolent glance By a similar process, heart sounds and murmurs can be analyzed individually and assigned their proper temporal relationship within the cardiac cycle The following routine has proved valuable in this regard

Selective Attention During Auscultation

The most convenient initial step is positive identification of the first heart sound If the

stethoscope is placed near the apex the timing of the first sound can be correlated with the precordial thrust When the identity of the first sound is definitely established attention should be confined to this sound alone during several successive cycles If the listener voluntarily blanks out all other sounds in the cycle the first sound can be subjectively isolated Several characteristics of the first sound should be noted individually and in sequence including intensity duration relative frequency or pitch, splitting etc The loudness of the sound must be interpreted in light of judgment concerning the transmission characteristics and hemodynamic situation of the individual subject *For example* a loud first sound in an obese subject has far greater significance than one of a similar intensity in an asthenic adult or a thin-chested youth The intensity of the vibrations is also affected by the vigor of ventricular contraction heart rate cardiac output P R interval and similar factors The relative intensity of the first and second sounds provides an additional clue concerning these factors

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around the primary areas It is frequently desirable to establish the relative intensities of the heart sounds and murmurs by going back over each area in quick succession, evaluating each sound in turn This is accomplished rapidly if the sounds have become familiar during the more careful *analysis in each area*

When this technique is recommended to medical students, they commonly express concern regarding their ability to accomplish this task In most cases, these doubts can be alleviated by suggesting that they produce schematic drawings of what they hear It is very helpful to compare such drawings with phonocardiograms or sonvelograms at first Even experienced examiners agree that the process of schematically drawing subjective impressions of sounds and murmurs can be a valuable experience

A second objection to systematic auscultation of the type described is the increased expenditure of time There is no doubt that this technique is more time consuming, particularly at first However, routine use of the method rapidly improves proficiency After a few weeks of concentrated effort, analysis of heart sounds and murmurs can become complete and accurate with little wasted time With experience it is possible to scan each phase of the cardiac cycle in turn by listening to only a few cycles during each step The time and effort spent are amply rewarded by striking improvement in accuracy of auscultatory diagnosis After years of unsystematic auscultation many examiners begin to recognize certain types *of murmurs for the first time by taking* advantage of dormant ability to focus attention on specific intervals of time

SUMMARY

Heart sounds and murmurs are audible vibrations emitted from the heart and great vessels Since the walls of the heart cannot vibrate without *setting the blood into vibration*, and vice versa, the origin of heart sounds was described in terms of oscillations induced by abrupt changes in velocity of the blood (due to closure of valves, etc) Heart murmurs occur in rapidly flowing blood and can be attributed to turbulence Turbulence occurs in fluids of low viscosity flowin rapidly through tubes of large caliber The velocity required to induce turbulence is greatly diminished by local obstructions in a tube, causing fluid to flow through a small orifice into a large channel or chamber Most heart murmurs can be readily explained on the basis of high velocity flow or abrupt changes in caliber of the vascular channels These mechanisms obviously apply to systolic and diastolic murmurs, produced by valvular deformities

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THE STANDARD LIMB LEADS

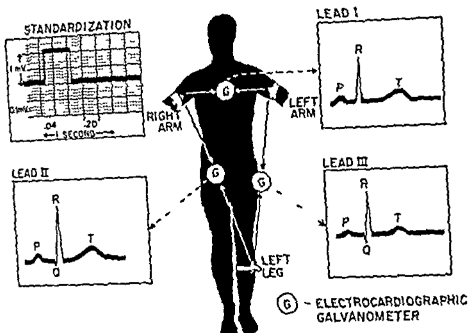


FIGURE 1 Electrocardiograms are recorded on paper divided into 1 mm and 5 mm. squares Standardization of the electrocardiograph is accomplished by adjusting its sensitivity until a potential of 1 mV produces a vertical deflection of 1 cm. The paper moves at a standard rate of 25 mm per second so 5 mm. along the horizontal axis represents an interval of 0 20 second and 1 mm indicates 0 04 second.

The standard limb leads consist of lead I lead II and lead III Lead I records the differences in potential between electrodes on the right and left arms In lead II the galvanometer is connected to electrodes on the right arm and left leg Lead III refers to connections between the left arm and left leg The polarity of these connections to the galvanometer is presented in Chapter 15

obtained by registering potential differences between the extremities as indicated in Figure 1

Electrical Manifestations of Atrial Excitation

A wave of excitation originating from the sino-atrial node and passing over the atria in the normal fashion produces a rounded deflection called the P wave Owing to differences in the sequence of excitation position of the heart and location of electrodes the P wave may assume many different shapes a few of which are indicated in Figure 2A After the atrial myocardium has been excited its excitability is gradually restored This return to the resting state is also accompanied by electrical potentials which may produce a very slight prolonged deflection called the T_a wave The T_a wave is usually obscured by the much larger potentials developed during ventricular excitation which normally follows atrial excitation by a brief interval

Electrical Manifestations of Ventricular Excitation

The atria are separated from the ventricles by the fibrous skeleton of the heart (see Fig 1 Chapter 1) Since this connective tissue barrier does not transmit waves of excitation the only excitatory pathway between the atria and ventricles is by way of the specialized conduction system which originates at the A-V node To emphasize the electrical isolation of atrial and ventricular myocardium the heart is schematically illustrated as consisting of two hollow masses of myocardium connected only by the bundle of His (see Fig 2C)

The wave of excitation passing over the

Chapter 14

Electrocardiographic Interpretation Abnormalities of Rate, Conduction and Rhythm

Many physicians leave electrocardiographic interpretation to cardiologists and rarely see the original records This attitude is unrealistic because considerable information can be gained from examining electrocardiographic records, even without specialized training Since electrocardiograms represent potentials inscribed on paper moving at a constant speed, the records indicate the rate and sequence of cardiac excitation Thus, heart rate can be accurately measured and abnormalities of rhythm and conduction can be readily identified This chapter will be devoted to the principles involved in detecting changes in rate, rhythm and sequence of cardiac excitation which can be mastered with little effort Electrocardiography becomes more complicated when changes in the shape of the individual deflections are analyzed Basic theories used to explain variations in the configuration of electrocardiographic complexes will be considered in Chapter 15

The sequence of cardiac excitation and the specialized conduction system of the heart were described in Chapter 1 (see Figs 4 and 6) The normal sequence of excitation initiates myocardial contraction and establishes the mechanical events of the cardiac cycle (Fig 7, Chapter 1) If the sequence of cardiac excitation and contraction is not clearly understood, the reader would profit by a review of those sections before proceeding

THE NATURE OF ELECTROCARDIOGRAMS

Electrical potentials associated with waves of excitation which spread through the heart can be recorded from electrodes applied to the surface of the body The electrodes consist of curved metal plates firmly applied to areas of skin which have been coated with electrode paste and gently abraded to reduce skin resistance The largest cardiac potentials recorded from the skin rarely exceed 2 mV, so very sensitive recording equipment is required for their registration String galvanometers, originally introduced by Einthoven for this purpose, have been almost completely replaced by direct writing galvanometers powered by vacuum tube amplifiers

Standardization

The sensitivity of the recording equipment is adjusted until a calibrating potential of 1 mV produces a vertical deflection of precisely 1 cm Thin horizontal lines on the paper are 1 mm apart and represent 0 1 mV, and the thick lines indicate 0 5 mV The recording paper routinely moves at a constant rate of 25 mm per second (approximately 1 in per second) The thin vertical lines demarcate intervals of 0 04 second (1/25 second) and the broad vertical lines indicate intervals of 0 20 second (1/5 second) Routine electrocardiography includes records

repolarization occurs more gradually than the excitation The shape of the T wave is quite variable and some of the common variants are indicated in Figure 2B Since ventricular excitation and the return to the resting state always occur in sequence every QRS complex must be followed by a T wave on at least two of the three standard limb leads (Fig 1)

The Normal Sequence of Excitation

On typical electrocardiograms P waves are followed after an interval by the electrical signs of ventricular excitation (QRS) and recovery (T) The duration of the various waves and of the intervals between them usually varies within fairly definite ranges in normal individuals Average values rounded to the nearest 0 04 second are indicated in Figure 3 The duration of the P wave ranges around 0 08 second During the interval between the end of the P wave and the beginning of the ventricular excitation (Q or R wave) the galvanometer remains at the baseline for about 0 08 second because no external potentials are recorded during

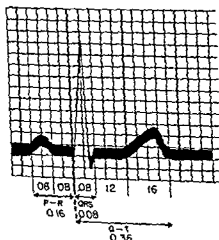


FIGURE 3 The average durations of electrocardiographic waves and intervals are rounded to the nearest 0 04 second so they are easier to remember The P R interval QRS interval and Q-T interval are among the most common values measured during routine electrocardiographic interpretation (see Figs 11 12 13)

the A-V nodal delay and the passage of the wave of excitation to the ventricular myocardium The QRS interval (0 08 second) represents the time required for waves of excitation to spread through the ventricular walls The flat segment between the end of the QRS complex and the beginning of the T wave (S-T interval 0 12 second) represents the period during which the ventricles are more or less uniformly excited and the T wave occurs during the restoration of the ventricular myocardium to the resting or excitable state

VARIATIONS IN HEART RATE

The heart rate is determined normally by the frequency with which the sino-atrial node emits excitatory impulses The frequency at which the S-A node discharges is influenced by activity of nerve fibers from the autonomic nervous system (see Chapter 6)

Measurement of Heart Rate

Since the electrocardiogram is an accurate representation of the intervals between successive cardiac cycles atrial and ventricular rates can be easily measured The simplest method is to determine the number of cycles (and fractions thereof) occurring in 3 seconds and multiply this number by 20 to give the number of cycles in one minute (60 seconds) (Fig 4) At the normal paper speed (25 mm per second) 1 second is represented by five large squares 3 seconds by fifteen large squares (3 in) The QRS complexes easily identified because of the rapid deflections are tallied over a 3 in distance If exactly four ventricular cycles occur during 3 seconds the ventricular rate is 80 per minute (see Fig 4) If the P waves can be identified the same process can be used to determine the atrial rate P waves can usually be differentiated from T waves which always follow QRS complexes at a fairly characteristic interval (see Fig 3)

Abnormalities of Heart Rate

Variations in the intensity of the sustained vagal tone have greater influence on the S-A

COMPONENTS OF ELECTROCARDIOGRAPHIC COMPLEXES

ATRIAL EXCITATION AND RECOVERY



VENTRICULAR EXCITATION AND RECOVERY

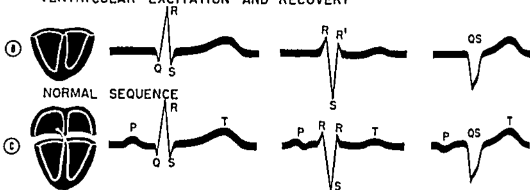


Figure 2 *A* Atrial potentials are illustrated as though excitation were confined to the atria A rounded P wave just precedes atrial contraction The T_a wave a shallow prolonged deflection in the opposite direction follows the preceding P wave and represents atrial repolarization Although a vast majority of P waves are rounded upward deflections they may assume many different shapes under both normal and abnormal conditions

B, Invasion of the ventricular myocardium by waves of excitation is attended by a group of rapid deflections called the QRS complex even though it may consist of only one or of several different spikes The components of the QRS complex are labeled arbitrarily (see text) The QRS complexes are followed by rounded prolonged T waves which signal the return of the ventricular myocardium to the resting state

C Normally the atrial excitation is followed after a brief pause by ventricular excitation so the P wave QRS complex and T wave appear in succession The QRS complex frequently obscures the T wave

atrium envelops the atrioventricular node and, after a slight delay, invades the specialized conduction system of the ventricles The excitatory process extends rapidly down these Purkinje fibers distributed over the endocardial surface of the ventricular chambers The mass of Purkinje fibers is so small that no external potentials are recorded until a wave of excitation is well established in the ventricular walls The ventricular conduction system provides a mechanism by which the entire endocardial surface of the ventricles is excited in very rapid succession and waves of excitation invade the ventricular walls almost simultaneously As the walls of the ventricular chambers are invaded, a series of rapid deflections can be recorded from the surface of the body The electrical signs of ventricular excitation may produce a wide variety of electrocardiographic patterns depending upon the position of the electrodes, the orientation of the heart and the sequence of excitation in the ventricular walls (see Fig 2*B*) The components of these complex deflections are labeled according to arbitrary rules If the initial rapid deflection is below the baseline, it is called a Q wave The first upward deflection is called an R wave The first downward deflection following an R wave is called an S wave When two upward deflections are present, the second is designated R Thus by definition, all upward deflections are R waves Occasionally no upward deflection appears and the entire complex consists of a broad downward deflection, designated QS The term QRS complex is usually applied to the rapid deflections accompanying ventricular excitation regardless of their configuration

After ventricular excitation is complete the galvanometer tracing normally returns to the baseline to be followed by a smoothly curved deflection (T wave) representing the final stages of the return to the resting state The T waves are generally smaller and broader than the QRS complex because

Pacemaker Activity in Myocardial Fibers

The functional differences between smooth muscle skeletal muscle and myocardium lie in the mechanisms for excitation and control (see Fig 2, Chapter 7) Under appropriate conditions all forms of muscle may exhibit myogenic excitation originating within the muscle itself For example the visceral smooth muscle in the ureter rhythmically contracts to produce peristaltic waves in response to myogenic impulses originating at a 'pacemaker' near the pelvis[1] If the ureter is sectioned below the normal pacemaker a new pacemaker is established below the transection and impulses are produced rhythmically at a somewhat slower rate Another transection lower down brings into play still another site of pacemaker activity with even slower inherent rate Occasionally a pacemaker region in the ureter exhibits impulse formation at a rate four or five times faster than the normal This phenomenon is reminiscent of the rapid rates of discharge in ectopic foci during paroxysmal tachycardia (*vide infra*)

If the heart of a chick embryo is sectioned between the common atrium and ventricle these two segments of myocardium may continue to contract rhythmically but the rate of ventricular contraction is slower than that of the atrium[2,3] Similarly excised myocardial tissue from mammalian hearts may contract repeatedly and here again the inherent rhythmicity of atrial tissue exceeds that of ventricular myocardium Every portion of the myocardium and conduction system can assume the role of pacemaker and initiate impulses conducted to contiguous regions At any moment the pacemaker of the heart abides in the region with the fastest inherent rate of impulse formation which is normally the sino-atrial node If impulses from the atria are blocked at the A-V node the atria continue to contract at their characteristic rate and another pacemaker in the ventricles emits impulses at a slower rate (30 to 60 beats per minute) When the pacemaker is situated in the ventricles impulses may be conducted in a retrograde direction to the atria or they may be blocked at the A-V node

The functional and electrocardiographic characteristics of arrhythmias are dependent upon four factors (*a*) All portions of the myocardium and conduction system are capable of originating waves of excitation (*b*) Functionally the heart consists of two double shells of myocardial fibers (atria and ventricles) joined by the common bundle of Purkinje fibers (Fig 5) (*c*) Owing to the syncytial arrangement of myocardial fibers, these waves of excitation spread to all contiguous myocardial cells (*d*) The wave of excitation pursues an abnormal course through some parts of the myocardium

Premature Contractions

The inherent capacity of all the myocardial fibers to rhythmically generate conducted impulses is not apparent so long as the sino-atrial node retains its position as pacemaker However impulses generated in regions other than the S-A node occur fairly often both in normal individuals and in patients with organic heart disease Changes occurring in regions of increased irritability (ectopic foci) have been the subject of considerable speculation with little or no direct experimental evidence It is fairly well established that myocardial fibers returning to their resting state after a cardiac contraction pass through a stage of increased excitability which appears to correspond to a similar state during the negative after-potential in nerve fibers[4] Conducted impulses originating at various sites in the ventricles tend to occur just after the T wave and the abnormal contractions follow closely behind the preceding beat. Such premature contractions per se have little or no clinical significance because they occur in a large proportion of normal individuals. Frequent premature contractions from multiple sites often occur with various types of heart disease The general location of the ectopic

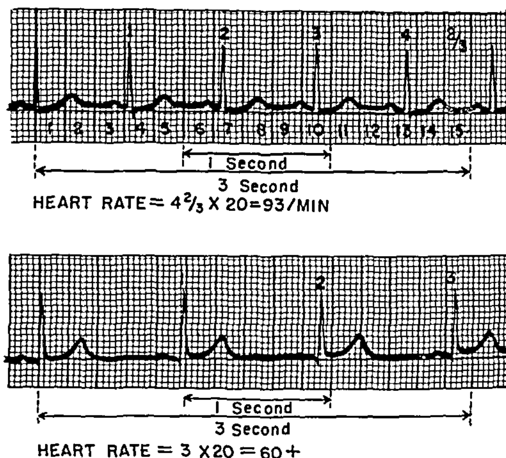


FIGURE 4 The heart rate in beats per minute can be computed by counting the number of cycles in 3 seconds and multiplying this value by 20 (3 × 20 = 60 seconds) At standard paper speed 3 seconds is represented by 15 large squares In the first example there are 4⅔ cycles in 3 seconds so the heart rate is about 93 per minute In the second example there are slightly more than 3 cycles in 3 seconds so the heart rate is a little over 60 per minute

node than does altered sympathetic activity (see Chapter 6) The slow heart rates found in certain athletes and during sleep, and the tachycardia found in fever, emotion and exercise, are attributed largely to variations in vagal tone Respiratory activity also may produce variations in vagal tone leading to phasic changes in heart rate with acceleration near the end of inspiration and slowing at the end of expiration This condition (*sinus arrhythmia*) is frequently encountered in normal individuals particularly when the heart rate is relatively slow

A heart rate faster than some arbitrary value (e g , 100 beats per minute) is termed *sinus tachycardia* if the impulses originate in the S-A node By the same token, a heart rate of sinus origin below some value (e g , 60 beats per minute) is called *sinus bradycardia* Intense vagal stimulation (e g from carotid sinus pressure) may transiently interrupt impulse formation by the sino-atrial node If such *sino-atrial arrest* is sufficiently prolonged, some other site in the heart may begin to discharge conducted impulses The fact that excitation of the heart can be initiated at any site in the myocardium or conduction system is the basic cause of cardiac arrhythmias

ABNORMAL RHYTHMS

Since abnormal rhythms of the heart usually result from variations in the site and frequency of impulse formation, the nature of pacemaker activity deserves special consideration

tion system had not fully recovered This is called *aberrant ventricular conduction* The abnormal wave of excitation in the atrium envelops the S-A node which cannot discharge another impulse until it has passed throu h its complete recovery cycle Thus the interval between an atrial premature contraction and the next normal beat is prolonged (compensatory pause in Fig 5) The salient features of atrial premature contractions are *altered configuration of the P wave* which clo.ely follows the T wave of the preceding normal contraction altered P R interval (usually diminished) normal or nearly normal QRS and T complexes and a compensatory pause The extent of the changes in P wave configuration and in the P R interval varies with location of the ectopic focus in relation to the *S-A node* If the wave of excitation originates from the region of the A V node the P waves are inverted and the P R interval is very brief (Fig 5)

Atrioventricular Nodal Premature Contractions Premature contractions may be initiated from an irritable focus in or near the *A V node* The wave of excitation passes immediately down the Purkinje system to the ventricles so a QRS complex closely follows the preceding normal T wave (Fig 5) Usually conduction into the atria is blocked and no P waves appear Occasionally a P wave begins just before the onset of QRS or is buried in the QRS complex indicating retrograde conduction into the atrial musculature Usually the ventricular excitation occurs in its normal sequence and the *form of the QRS complex is similar* to the patterns displayed during normal cycles In the absence of retrograde conduction into the atria the rhythm of the S-A node is undisturbed and the interval between the normal cycles preceding and following the premature contraction is equal to that of two normal cycles In other words the short interval before the premature contraction is precisely balanced *by the greater delay following* the abnormal beat (completely compensatory pause) The characteristic signs of A V nodal premature contractions are the appearance of normal or relatively normal QRS complexes appearing just after the preceding T wave with P waves either absent buried in the QRS complex or beginning just before the premature QRS

Ventricular Premature Contractions If an ectopic focus within the ventricular musculature discharges prematurely, the course of the wave of excitation and the sequence of ventricular depolarization are abnormal and the configuration of the QRS complex is *correspondingly* distorted Since ectopic foci can develop at any site in the ventricles an infinite variety of complexes may *result*

The typical electrocardiographic picture consists of slurred prolonged QRS complexes beginning without a P wave just after the termination of the *preceding normal* cycle Repolarization occurs in an abnormal sequence and the T waves are also deformed tending to deflect in a direction opposite to the major QRS deflection (Fig 5) When an ectopic focus is located near the base of the heart at some distance from the conduction system the general course of the wave of excitation extends from base to apex, and the *major* QRS deflections are upward *in* all standard limb leads as in a normal cycle In contrast a premature ventricular contraction originating near the apex is characterized by the spread of excitation from the apex toward the base of the heart and the *major QRS deflections* are downward in all *standard* limb leads (Fig 5) A completely compensatory pause *follows* the typical *premature* ventricular contraction just as in the A-V nodal ectopic beats

Premature ventricular contractions recurring regularly after every normal cycle, may persist for extended periods of time These premature contractions are termed *coupled* beats and the resulting rhythm is called *bigeminy* because two pacemakers alternate in discharging excitatory impulses to the ventricular myocardium In a few patients with slow heart rates premature ventricular contractions are regularly interposed between normal beats without a compensatory pause

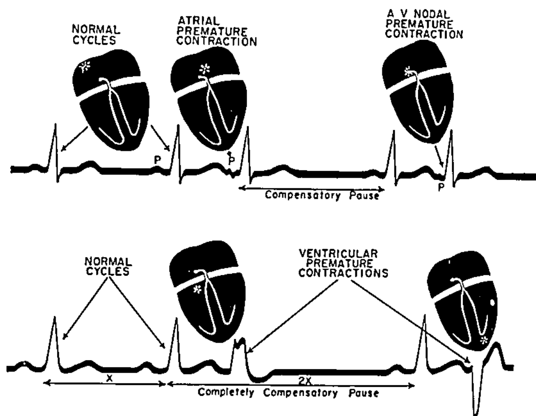


FIGURE 5 Premature contractions can originate at ectopic foci in any portion of the atria or ventricles A few examples are illustrated schematically

Atrial premature contractions begin with a deformed P wave shortly after the T wave of the preceding normal cycle The P R interval is usually shortened but the QRS complex is characteristically unchanged in configuration The interval between the premature contraction and the next normal cycle is somewhat prolonged (compensatory pause)

Premature contractions originating at the A V node are similar to atrial premature contractions except that the P wave is largely buried within the QRS complex since the atria and ventricles are excited more or less simultaneously

Ventricular premature contractions are characterized by markedly deformed and prolonged QRS complexes with no definite S T segment and with the T wave deflected in a direction opposite to the major deflection of the QRS P waves are not visible

focus giving rise to these premature contractions can usually be determined electrocardiographically (see Chapter 15)

ATRIAL* PREMATURE CONTRACTIONS If an irritable focus in the atrium generates a conducted impulse very soon after the preceding contraction, the wave of excitation spreads out concentrically from this new site (Fig 5) The course of the wave of excitation is different from that of an impulse arising in the sino-atrial node and therefore the shape of the P wave is altered The time required for the atrial wave of excitation to engulf the A-V node is different, so the P R interval also varies from that of the preceding normal beat The QRS and T waves are generally unchanged because the excitatory impulse follows a normal course from the A-V node through the ventricular myocardium and repolarization of the ventricles is usually not affected However, in some cases slight changes in the configuration of QRS and T waves are produced, probably because the impulse followed the previous excitation so closely that some portion of the conduc

* The word *auricle* has been widely used as though it were a synonym for *atrium* Anatomically *auricle* refers to an atrial appendage and is not appropriate for indicating the main atrial chamber To avoid inconsistency the correct term will be used in spite of traditional usage in such familiar conditions as auricular premature contractions auricular fibrillation etc

absent. Successful therapy by carotid sinus pressure or other procedures producing vagal discharge represents a diagnostic test for atrial or A-V nodal tachycardia. It may be difficult to differentiate atrial and nodal paroxysmal tachycardia because P waves may be obscured by T waves when the cycle length is short. This poses no practical problem since the functional significance and therapy of these two conditions are similar. The prolonged and bizarre QRS complexes which occur with ventricular paroxysmal tachycardia simplify its recognition (Fig. 7).

FUNCTIONAL SIGNIFICANCE OF PAROXYSMAL TACHYCARDIA. Short bursts of premature ventricular contractions produce changes in systolic and diastolic circumference of the heart and in the energy release (Fig. 8) which are similar to those with individual premature ventricular contractions (Fig. 6). The stroke volume is apparently diminished significantly during the paroxysms of tachycardia. With a constant rapid heart rate cardiac reserve must be diminished. It is interesting to note that exercise eliminated the paroxysms of tachycardia in the experiment illustrated in Figure 8. The deleterious effects of tachycardia on cardiac efficiency and on coronary blood flow have been discussed in Chapter 8. It is therefore not surprising that patients developing persistent ectopic tachycardia of this type suffer limitation in exercise tolerance and may even develop acute congestive failure when the heart is diseased (Chapter 9). For example Grant[5] described an episode of paroxysmal auricular tachycardia in a 20-year-old army private, previously found to have an average exercise tolerance by tests at the Harvard University Fatigue Laboratory. About four months later he noted "pounding of the heart" during a routine 30-mile hike. Tachycardia at a rate of about 200 per minute persisted until the next day when he had definite signs of congestive heart failure. In spite of numerous attempts to interrupt the attack of tachycardia, the patient died after 40 hours. Postmortem examination revealed unsuspected mitral stenosis.

TYPES OF PAROXYSMAL TACHYCARDIA

A ATRIAL PAROXYSMAL TACHYCARDIA





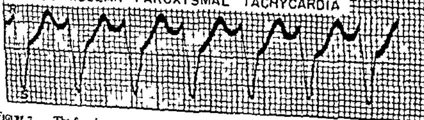


FIGURE 7. The fact that paroxysmal tachycardia actually represents a series of premature contractions is clearly indicated by comparing atrial, A-V nodal and ventricular paroxysmal tachycardia with corresponding isolated premature contractions in Figure 5.

FUNCTIONAL EFFECTS OF PREMATURE CONTRACTIONS

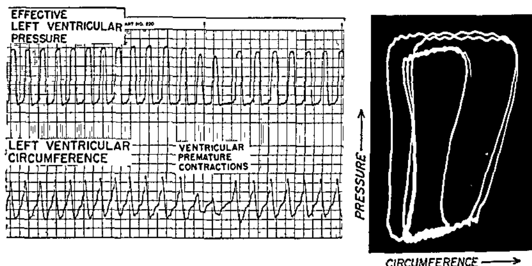


FIGURE 6 Ventricular premature contractions begin before diastolic filling is complete and the degree of systolic ejection is less than normal Although systolic ventricular pressure is elevated almost to the normal levels the volume ejected by these abnormal contractions is markedly reduced The area of the pressure circumference loops was markedly diminished indicating that the work accomplished by the myocardial fibers involved was greatly curtailed

These ectopic beats are called *interpolated* premature ventricular contractions

The effects of ventricular premature contractions on energy release Ventricular premature contractions in experimental animals were characterized by diminished diastolic filling and incomplete ventricular ejection (Fig 6) Thus, the area of the pressure-circumference loops was diminished even when the ventricular systolic pressure approached the same height as the normal cycles A very brief filling time may account for the reduced diastolic distention of the ventricles The diminished systolic ejection may be due to asynchronous contraction of the various myocardial bundles of the ventricular walls

Paroxysmal Tachycardia

A burst of three or four ectopic impulses is generally classed as multiple premature contractions However, an ectopic focus may discharge a long series of premature contractions in rapid succession at rates higher than 140 per minute (Fig 7) Such sustained ectopic pacemaker activity lasting minutes or days is called paroxysmal tachycardia This arbitrary distinction between premature contractions and paroxysmal tachycardia indicates the close functional relation between them Ectopic foci producing either isolated premature contractions or paroxysms of tachycardia may develop anywhere in the heart In a typical attack of paroxysmal tachycardia the heart rate is abruptly elevated to levels of 140 to 240 beats per minute most commonly around 160 per minute *Once attained, this rapid rate is exceedingly regular,* and is essentially unaffected by respiratory activity, exercise, or other controlling mechanisms until the attack is abruptly terminated

Clinical diagnosis of *paroxysmal tachycardia* depends upon a history of a very fast extremely regular heart rate which begins abruptly and does not change until it suddenly reverts to normal Paroxysmal tachycardia originating from sites in the *atria or* A-V node is often terminated promptly by inducing intense vagal discharge (pressure on the carotid sinus deep inspiration with mild Valsalva maneuver induced vomiting pressure on the eyeballs etc) *These procedures* generally have no effect on an ectopic pacemaker in the ventricular walls, which suggests that parasympathetic distribution to the ventricular myocardium is scanty or

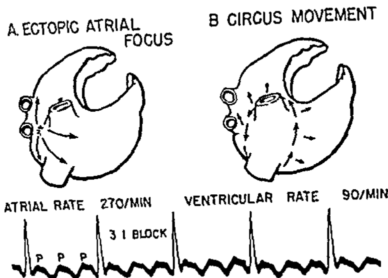


FIGURE 9 Atrial flutter is characterized by repetitive atrial excitation occurring at such a rapid rate that all waves of excitation are not transmitted through the A V node into the ventricles Thus there may be two P waves for each QRS complex (2 1 block) three P waves to one QRS (3 1 block) or even 4 1 block.

A In recent years the rapid atrial rate has been ascribed to the rapid firing of an ectopic focus in the atrial musculature similar to atrial paroxysmal tachycardia except for the failure of the A V node to transmit all the impulses

B Formerly atrial flutter was described as a wave of excitation encircling the roots of the superior and inferior vena cava at a rate determined by the conduction velocity of the myocardium Waves of excitation spread from the circular pathway to the remainder of the atrial musculature Circus movements of this type can be produced experimentally (see text)

or in other complexes can generally be detected by carefully inspecting the record at a point just half way between the clearly defined P waves A pair of calipers adjusted until the distance between the points is just half the distance between obvious P waves is often helpful in the procedure

The functional significance of atrial flutter depends ultimately upon the ventricular heart rate If the A-V node transmits alternate atrial impulses (2 1 A-V block) the ventricular rate is very rapid (e g 150 beats per minute) Under these conditions the diastolic filling interval for the ventricles is seriously curtailed and the resulting condition closely resembles paroxysmal atrial tachycardia (*vide supra*) If 3 1 or 4 1 block persists during various levels of activity the heart rate remains relatively fixed at levels of 70 to 100 beats per minute at rest and the cardiac reserve is curtailed during exertion because tachycardia does not occur

Atrial Fibrillation

If more than one wave of excitation were moving over the atrium at all times coordinated atrial contraction could not occur and individual P waves could not be identified on electrocardiograms Instead the P waves would be replaced by irregular oscillations of the baseline fibrillation waves A similar situation would result from multiple ectopic atrial foci discharging asynchronously at rapid rates Here again a number of postulates have been advanced (Fig 10) but the ultimate answer must await further evidence In any event waves of excitation arrive at the A-V node at random intervals Only a portion of these excitatory waves are transmitted to the ventricles Some excitatory waves are too weak or diffuse to invade the A-V node and others arrive during its refractory period By this mechanism the ventricular rate is absolutely irregular since the A-V node receives its excitation in a

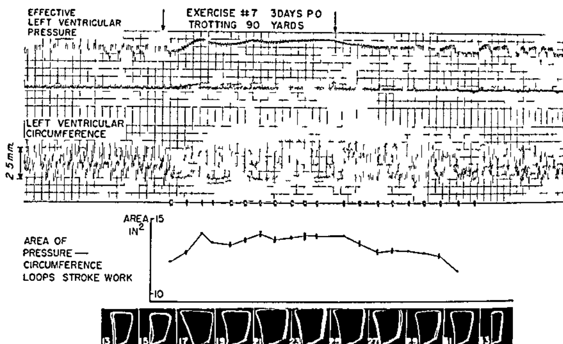


FIGURE 8 Frequent short bouts of ventricular paroxysmal tachycardia were noted in an experimental animal three days after the installation of pressure and circumference gauges The principal change was a diminution in ventricular systolic pressure (above) and reduced diastolic filling and systolic ejection (below) During exertion and for a short time thereafter the paroxysmal tachycardia disappeared

Atrial Flutter

Very rapid regular atrial excitation can be produced experimentally by a wave of excitation continuously following a circular pathway in the atrial musculature around some obstruction (e g around the roots of the superior and inferior venae cavae) This "circus movement' can be produced by damaging the atrial myocardium between the superior and inferior venae cavae and electrically stimulating the atrium to induce a wave of excitation which circles the obstruction at a rate determined only by the conduction velocity of the myocardium and the circumference of the circle [6] From this circular pathway excitation spreads to the remainder of the atrium and to the A-V node (Fig 9*B*) Thus, the atria are excited at rates of 150 to 350 times per minute Apparently the A-V node is unable to respond to repetitive excitation at these high rates and transmits alternate impulses (2 1 block) every third impulse (3 1 block) or every fourth impulse (4 1 block), depending upon its recovery time The concept that atrial flutter observed in patients was due to a circus movement in the atria held sway for many years but recently a large body of evidence has been presented indicating that atrial flutter is due to rapid, repetitive excitation from a single ectopic focus (Fig 9*A*) This conclusion discussed in detail by Scherf and Schott[7] and by Prinzmetal et al,[8] implies that atrial flutter must be considered comparable to paroxysmal tachycardia except that the atrial waves of excitation occur at a rate which is faster than the A-V node can transmit impulses The electrocardiographic signs of atrial flutter can be predicted from either of these descriptions even though the etiology of the condition remains controversial [9] The ventricular rate is usually regular although a shift from one degree of block to another may occur The major difficulty in interpreting the records stems from the fact that the P waves tend to be superimposed upon the T waves If this fact is not recognized half of the P waves may be overlooked, leading to erroneous conclusions P waves hidden in T waves

Clinical Significance of Arrhythmias

The preceding discussion of arrhythmias does not represent a comprehensive coverage of the subject but illustrates the type of logic which leads to their identification. The presence of arrhythmia does not necessarily indicate heart disease. Premature contractions and paroxysmal tachycardia occur in hearts which have no demonstrable pathologic changes in subsequent postmortem examinations. On the other hand, they are more frequently found in patients with organic disease. Certain arrhythmias are more likely to be associated with particular types of heart disease. For example, atrial fibrillation is frequently encountered in patients with hyperthyroidism or with left atrial dilatation from stenosis of the mitral valve. Premature contractions often originate in portions of the myocardium in which the blood supply is insufficient (e.g., from obstruction of coronary arteries). In any case abnormal rhythms must be evaluated along with all other available evidence to arrive at a judgment concerning the cardiac status of the patient.

ABNORMAL CONDUCTION

Since the atrium contains no specialized conduction system, waves of excitation are rarely delayed during their spread over the atrial musculature. A very common site of delayed conduction occurs at the transition between the atrial myocardium and the atrioventricular node. Indeed, some A-V nodal delay occurs normally and is frequently prolonged by inflammatory and toxic effects on the heart (see Chapter 17).

Disturbances of Atrioventricular Conduction

Theoretically, delay in the excitation of the A-V node might be detected by measuring the interval between the end of the P wave and the beginning of the ventricular complex (QRS). However, variability in the duration of the P wave limits the accuracy of this measurement. Instead, the time elapsing between the beginning of the P wave and the beginning of ventricular excitation (Q or R wave) is measured. This interval (P-R) includes the A-V nodal delay and is routinely used to detect its prolongation (Figs. 3 and 11).

The P-R interval averages about 0.16 second but varies with age and with heart rate (Table 3). This interval includes the time required to excite the atria, the A-V nodal delay and conduction along the common bundle and bundle branches to the ventricular myocardium. The upper limits of normal for the P-R interval vary from 0.20 second in an adult with an average heart rate (72 per minute) to 0.125 second in an infant with a fast heart rate (e.g., 160 per minute) as indicated in Table 3. According to Kossmann[11] such tables are unnecessary if one remembers that the upper limit of normal in adults is 0.20 second; in adolescents between the ages of 14 and 17 years, the P-R interval should remain below 0.18

TABLE 3. UPPER LIMITS OF THE NORMAL P-R INTERVAL*

RATE	BELOW 70	71–90	91–110	111–130	ABOVE 130
	sec.	sec.	sec.	sec.	sec.
Large adults	0.21	0.20	0.19	0.18	0.17
Small adults	0.20	0.19	0.18	0.17	0.16
Children, ages 14 to 17	0.19	0.18	0.17	0.16	0.15
Children, ages 7 to 13	0.18	0.17	0.16	0.15	0.14
Children, ages 1½ to 6	0.17	0.165	0.155	0.145	0.135
Children, ages 0 to 1½	0.16	0.15	0.145	0.135	0.125

* From Ashman, R., and Hull, E.: Essentials of Electrocardiography, 2nd ed. New York, The Macmillan Co., 1945.

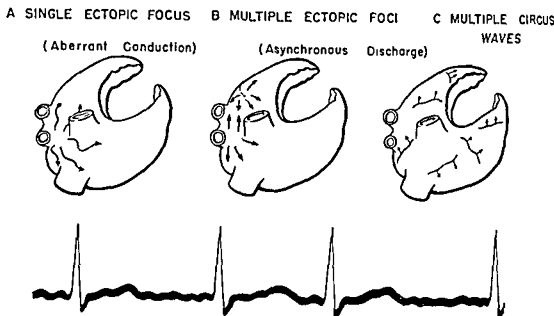


FIGURE 10 Atrial fibrillation is characterized by a totally irregular ventricular rhythm The A V node transmits impulses in a completely random fashion apparently because impulses arrive in its vicinity at varying intervals At least three explanations for this condition can be advanced

A A single ectopic focus may discharge impulses at such a vary rapid rate that portions of the atrial muscle are refractory Thus the waves of excitation are broken up and follow aberrant pathways irregularly over the atrial musculature

B Multiple ectopic foci discharging asynchronously at high rates would produce an apparently random distribution of excitatory processes traveling through the atrial walls

C Multiple waves of excitation could follow random courses through the atrial myocardium following pathways where the myocardium has returned to the excitable state This concept is an extension of the circus movement theory for atrial flutter

completely random sequence The complete lack of ventricular rhythm can be readily perceived by palpation of the radial pulse or auscultation over the precordium Electrocardiographic signs of atrial fibrillation are illustrated in Figure 10

The principal functional disturbance produced by atrial fibrillation is the elimination of effective atrial contractions Multiple waves of excitation traversing the atrial musculature produce uncoordinated contraction waves which change the shape of the chamber but produce no concerted evacuation of blood into the ventricles Loss of atrial contribution to ventricular filling may not be very important at rest However the reserve capacity of the heart may be significantly restricted by elimination of atrial contraction at the proper interval before ventricular contraction and by uncontrolled irregular rhythms The extent to which stroke volume is limited by atrial fibrillation is not known but it could be very important Furthermore, neural control of ventricular rate is lost and the cardiac reserve is diminished by the lack of compensatory tachycardia

Ventricular Fibrillation

A random distribution of excitatory waves traversing the ventricular musculature would preclude a coordinated ventricular contraction just as it does in the atrium Thus ventricular fibrillation can be survived for only brief periods and is a common immediate cause of death Thus electrocardiographic records of ventricular fibrillation are rarely obtained They consist of broad irregular waves of varying amplitude and configuration Transient bouts of ventricular fibrillation are occasionally responsible for periodic fainting reactions

second and in children under 14 years below 0 16 second

PROLONGED P R INTERVAL (FIRST DEGREE ATRIOVENTRICULAR BLOCK) The P R interval should be measured on the lead in which a prominent Q wave occurs and the P wave is well formed If the Q wave is absent, the lead with the longest QRS interval should be used In most cases these criteria are best met in lead II When the measured P R interval exceeds the upper limits of normal an electrocardiographic diagnosis of prolonged P R interval or first degree A-V block is indicated (Fig 11*A*) Since a number of different conditions may produce prolongation of the P-R interval this electrocardiographic sign does not imply either an etiologic or an anatomic diagnosis of the conditions which produced it However prolonged P R intervals occur quite frequently in the course of acute rheumatic fever (see Chapter 17)

The functional significance of first degree atrioventricular block Prolongation of the P R interval occurs most frequently in the course of inflammatory disease processes involving the entire myocardium (e g acute rheumatic fever) This being the case the principal functional disturbances are due to the underlying disease process which caused the delayed A V nodal conduction (see Chapter 17) In addition, a prolonged interval between atrial and ventricular systole may deleteriously affect closure of the mitral and tricuspid valves During atrial contraction blood is driven into the already distended ventricular chambers and the atrioventricular valves move toward the position of closure If ventricular systole is delayed the valves gape wide again and some of the blood ejected by atrial systole probably flows back into the atria When ventricular systole begins the valves are separated and an increased degree of regurgitation occurs before the valves are closed and sealed (see Chapter 13) The effectiveness of atrial contraction in producing ventricular filling is also reduced in other forms of A V block (*vide infra*)

PARTIAL ATRIOVENTRICULAR BLOCK (SECOND DEGREE ATRIOVENTRICULAR BLOCK) More severe degrees of A V block may produce occasional or regularly recurring dropped ventricular beats For example in some patients, the P R interval becomes progressively longer in a sequence of cycles until a point is reached at which a P wave is not followed by a QRS complex (Wenckebach phenomenon) In this particular cycle the spreading wave of atrial excitation is blocked at the A V node and fails to reach the ventricles In other cases an occasional ventricular complex is missing without a change in the P R interval (Fig 11*B*)

COMPLETE ATRIOVENTRICULAR BLOCK. If all atrial waves of excitation fail to pass the A V node a pacemaker in the ventricle must *be established* The inherent rhythmicity in the ventricular conduction system or myocardium is characteristically much slower than that of the A-V node or the atrial musculature generally ranging from 40 to 60 impulses per minute Under these conditions the atria and ventricles are excited by independent pacemakers discharging at very different rates The P waves occur regularly and with a frequency almost double that of the QRS complexes but the two chambers are sufficiently out of phase so that the P-R intervals are continuously variable and have no meaning If the ventricular excitation originates in the immediate vicinity of the A V node the course of excitatory impulses to the ventricular muscle is along the normal pathways and the QRS complex is essentially normal in duration and configuration On the other hand excitation spreading from an ectopic pacemaker somewhere in the ventricular myocardium will of necessity follow an abnormal and more devious course, producing alterations in both configuration and duration of the QRS interval

PREMATURE ATRIOVENTRICULAR CONDUCTION (WOLFF PARKINSON-WHITE SYNDROME) In 1930, Wolff Parkinson and White[12] described a syndrome characterized by (1) shortening of the P R interval usually to 0 12 second or less (2) prolongation of the

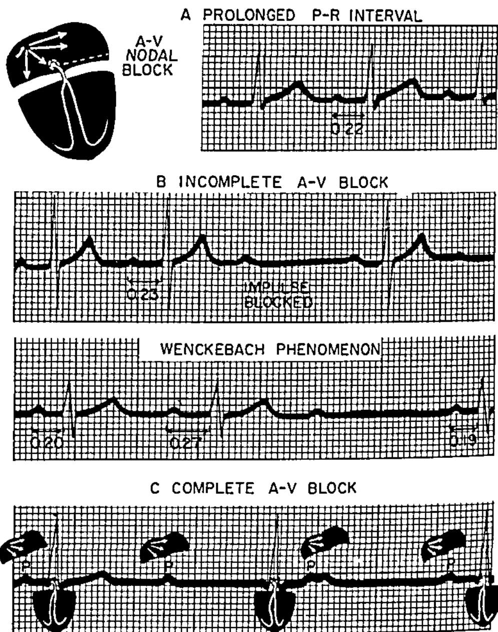


FIGURE 11 *A* Prolongation of the P R interval implies increased delay in conduction between the atrial myocardium and the A-V node (A-V nodal delay) This condition is called merely *prolongation of P R* or sometimes *first degree A V block*

B When A V nodal conduction has been impaired an atrial wave of excitation may occasionally fail to invade the A V node and no QRS complex follows the normal P wave This is called *partial A V block* Occasionally the P R interval becomes progressively longer and longer with each successive cycle until an impulse is blocked at the A-V node (*Wenckebach phenomenon*)

C Complete A V block implies that none of the normal atrial waves of excitation pass the A V node to enter the ventricles Under these conditions another pacemaker becomes established in the ventricle which usually generates impulses at a slower rate The ventricular pacemaker is often situated at or near the A V node as indicated above and the QRS complexes remain normal If the QRS complexes are slurred and deformed as occurs with ventricular premature contractions (Fig 5) the ventricular pacemaker is somewhere in the ventricular myocardium The atrial and ventricular rates are completely independent

of two patients They postulated that an irritable focus at the tip of the catheter was being discharged by the increased intra ventricular pressure following atrial systole (Fig 12B) More recently Prinzmetal et al[15] advanced the theory that accelerated conduction along the normal pathways could produce the Wolff Parkinson-White syndrome (Fig 12A) They presented evidence that the duration of A-V nodal delay could be diminished greatly Assuming that it requires 0 07 second for the wave of excitation to pass from the S-A node to the A V node a P R interval of 0 19 second would suggest an A V nodal delay of some 0 12 second When the P R interval is reduced to 0 11 second the A V nodal delay might be only 0 04 second (0 11 − 0 07 = 0 04) It is too early to evaluate this concept so the reader is referred to their monograph on accelerated conduction[15] and to a review of the current status of the subject by Wolff[16]

Disturbances of Ventricular Conduction

Rapid conduction of the excitatory impulse over the Purkinje system provides almost simultaneous distribution of waves of excitation to the endocardial surfaces of both ventricles Since excitation normally reaches all parts of the ventricular wall within a very brief interval the potentials develop rapidly and end promptly producing QRS complexes of short duration and deflections which are sharp and clean If the excitation of any large portion of the ventricle is delayed the duration of the QRS complex is increased and the configuration is altered by slurred notched multiphasic or prolonged deflections in various leads (Fig 13) Despite the fact that an almost endless variety of QRS configurations can be produced by different alterations in ventricular conduction an electrocardiographic diagnosis of intraventricular conduction disturbance (intraventricular block) can be made whenever the QRS interval exceeds certain arbitrary values

The QRS interval is measured from the point at which the first deflection (Q or R wave) leaves the baseline to the termination of the complex It should be measured in the standard limb lead in which it is longest An average value for QRS interval in adults is about 0 08 second The maximal normal QRS interval is approximately 0 10 second in adults 0 09 second in children from 5 to 14 years of age and 0 08 second in children under 5 years of age[11] Although the electrocardiographic diagnosis of defective intraventricular conduction is readily made, its clinical significance requires analysis of the type and location of the disturbance The nature and extent of abnormal ventricular conduction can be assessed only by an analysis of the configuration of the QRS complexes in various leads (see Chapter 15)

THE DURATION OF ELECTRICAL SYSTOLE (Q-T INTERVAL) The interval occupied by the QRS-T complex represents the time required for excitation and repolarization of the ventricular myocardium The so-called Q-T interval is measured from the beginning of the QRS complex (Q or R wave) to the end of the T wave (Fig 3) The Q-T interval varies somewhat with heart rate age and sex so it is generally necessary to refer to a table to determine if a particular value is within normal limits or exceeds the upper limit of normal (see Table 4) Accurate

ABNORMAL INTRAVENTRICULAR CONDUCTION

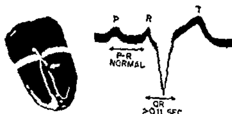
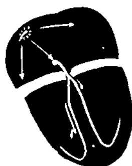
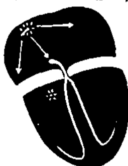
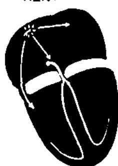


FIGURE 13 Blocked or delayed conduction in major branches of the Purkinje system produces asynchronous excitation of the ventricular walls Since the wave of excitation follows a normal course from the S-A node through the A V node the P waves and the P R interval are normal. Delayed excitation of a major portion of the ventricular walls produces prolonged, bizarre QRS complexes The types and significance of ventricular conduction disturbances are considered further in Chapter 15

PREMATURE ATRIOVENTRICULAR CONDUCTION
(Wolff-Parkinson-White Syndrome)







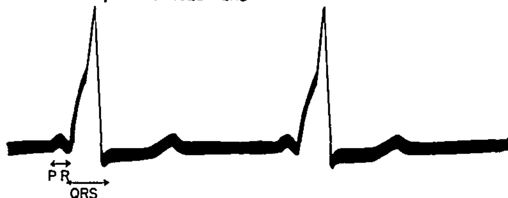


FIGURE 12 The Wolff Parkinson White syndrome is characterized by shortened P R intervals with prolonged and distorted QRS complexes Three concepts have been invoked to explain this phenomenon

A According to one recent theory the normal delay at certain portions of the A V node is greatly diminished so that conduction to corresponding areas of ventricular myocardium is accelerated (see text)

B An irritable focus in the ventricular myocardium discharged by atrial contraction could produce the typical electrocardiographic patterns

C An older theory was based on myocardial bridges between the atria and ventricles (bundles of Kent) which had been observed in very young experimental animals Ventricular excitation along the normal and abnormal pathways could theoretically produce the prolonged and abnormal QRS complexes

QRS interval, usually to 0 10 second or more and (3) a susceptibility to bouts of *atrial paroxysmal tachycardia and other arrhythmias* (premature contractions atrial flutter and atrial fibrillation) The so-called Wolff-Parkinson-White syndrome has been attributed to a number of theoretical causes of which three will be mentioned Kent[13] described muscular bundles connecting the atria and ventricles in young rats and rabbits A wave of excitation passing over the atrium might traverse these bundles of Kent and initiate excitation in the ventricles at an abnormal site during the A-V nodal delay (Fig 12*C*) Under these circumstances the QRS complex should begin very soon after the P wave (shortened P-R interval) and excitation over the normal conduction pathways *would complete ventricular excitation* Thus, the QRS interval would persist during the aberrant excitation and the excitation along normal pathways (prolonged QRS) However, myocardial bridges between atrium and ventricles cannot be consistently located in man and certainly cannot be correlated with the Wolff-Parkinson White syndrome, since electrocardiographic signs of this disturbance may appear and disappear at varying intervals Kossmann et al[14] reported that electrocardiographic complexes characteristic of the Wolff-Parkinson-White syndrome were produced during catheterization

two cycles in rapid succession followed by a slightly prolonged interval or compensatory pause A P R interval in excess of the maximal normal values presented in Table 3 means a first degree A V block or increased A V nodal delay Regularly recurring cycles consisting of a P wave without a QRS T complex signify partial A V block (second degree A V block) A continuously variable P R interval suggests complete A V block

The QRS interval is measured as indicated in Figure 3 and if this value exceeds 0 10 second in adults with normal heart rates an interventricular conduction disturbance is present When P waves precede the prolonged QRS complexes by normal intervals conduction within the ventricles is delayed or blocked If P waves are absent and the ventricular rate is very regular at rates in excess of 140 per minute at rest and the QRS complexes are prolonged and bizarre the diagnosis is ventricular paroxysmal tachycardia Very slow ventricular rates (less than 60) with P waves absent or buried in a prolonged bizarre QRS complex imply sinus block with an ectopic pacemaker in the ventricles

If the process of cardiac excitation can be clearly visualized and the P QRS and T waves can be identified on the records most of the common disturbances of rhythm and conduction can be recognized with little effort More complete analysis particularly as it involves interpretation of the changes in shape of the various portions of the record can best be approached with an understanding of the basic principles of electrocardiographic theory summarized in Chapter 15

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TABLE 4 UPPER LIMITS OF THE NORMAL Q-T INTERVAL*

HEART RATE PER MIN	MEN & CHILDREN	WOMEN
	sec	sec
40	0 491	0 503
43	0 479	0 491
46	0 466	0 478
48	0 460	0 471
50	0 453	0 464
52	0 445	0 456
54 5	0 438	0 449
57	0 430	0 441
60	0 422	0 432
63	0 413	0 423
66 5	0 404	0 414
70 5	0 395	0 405
75	0 384	0 394
80	0 374	0 384
86	0 363	0 372
92 5	0 351	0 360
100	0 338	0 347
109	0 325	0 333
120	0 310	0 317
133	0 294	0 301
150	0 275	0 282
172	0 255	0 262

* From Ashman R and Hull E Essentials of Electrocardiography 2nd ed New York The Macmillan Co 1945

measurement of the Q-T interval is more complicated than it appears For this reason Kossmann[11] pointed out the futility of listing normal values to three significant figures when errors of 5 to 12 5 per cent occur even when 3 to 12 cycles are measured He recommended that the maximum normal Q-T interval (corrected for heart rate) for any age or sex be set at 0 425 Any value above this level should be described as a prolonged Q-T_c but may not necessarily be abnormal' A large number of factors are known to alter the Q-T interval Although prolongation of the Q-T interval has been advocated as an important sign of toxic or inflammatory conditions in the myocardium (e g , acute rheumatic fever) this measurement has not been particularly useful in my experience (see also Fig 10 Chapter 17)

SUMMARY

Electrocardiographic signs of abnormal heart rate, rhythm and conduction were summarized briefly to illustrate the kind of logic which can be applied to an analysis of electrocardiograms Electrocardiographic interpretation was introduced in this way to demonstrate that information can be gleaned from electrocardiographic tracings on logical grounds It was not considered appropriate to attempt an exhaustive discussion in a text of this sort Additional details should be sought in standard textbooks of electrocardiography[10 17-19] With a little experience following a simple routine will disclose most of the common types of abnormal heart rates, arrhythmias and conduction disturbances

Procedure for Detecting Abnormalities of Heart Rate, Rhythm and Conduction

Analysis of electrocardiograms should begin with the following steps

1 Determine ventricular rate and atrial rate
2 Examine the record for variations in rhythm
3 Examine the complexes to detect changes in configuration
4 Measure P-R interval and compare with Table 3
5 Measure QRS interval

Determining ventricular rate is the first step in analyzing an electrocardiogram If a P wave precedes each QRS complex by a constant interval the atrial rate is the same as the ventricular rate The P-R interval is measured in several complexes and if this value is relatively constant and within the range of normal, the rhythm is probably of sinus origin In adults, heart rates below 60 can be termed sinus bradycardia and above 100 are labeled sinus tachycardia If the heart rate is absolutely constant at levels above 140 at rest and the QRS complex is normal, the diagnosis is atrial paroxysmal tachycardia when P waves precede the QRS complexes by a normal interval If P waves cannot be distinguished the term supraventricular (atrial or A-V nodal) paroxysmal tachycardia is applied Premature contractions are identified while scanning the records by noting

Action Potentials

If the membrane potential is diminished to some critical level in a local area either spontaneously or by an external electrical stimulus the permeability of the membrane to sodium and potassium increases suddenly permitting these ions to pass through the membrane [3,4] This process rapidly reduces and then reverses the membrane potential At the same time current flowing into the depolarized portion of the membrane passes out through adjacent regions of the cell membrane This local current flow is sufficient to depolarize these adjacent regions and produce propagation of the impulse down the fiber In this way a wave of increased permeability (with its associated changes in membrane potential) spreads rapidly down the myocardial fiber The fiber is restored to the resting state when membrane permeability to sodium and potassium returns to normal and the unequal ion distribution again becomes manifest

The rapidly propagating area of increased membrane permeability produces a flow of electrical current and changes in potential which can be recorded from an intracellular electrode (Fig 1) As the wave of excitation passes the electrode at a velocity of about 0 3 m per second, the membrane potential decreases and reverses very rapidly (the inside of the cell becomes positive with respect of the outside) Thus, an active myocardial cell is not only depolarized but actually exhibits an overshoot to a positive potential The membrane potential returns toward the resting value slowly at first and then very rapidly

Action potentials measured from single myocardial cells bear little resemblance to cardiac potentials recorded from the surface of the body These differences must be

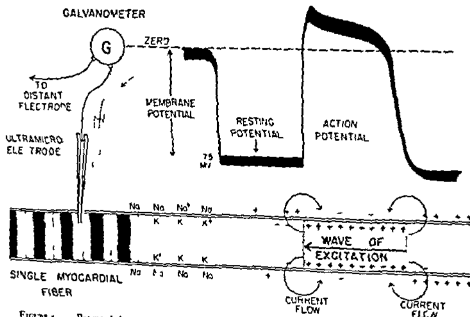


FIGURE 1 Potentials between the inside and outside of myocardial cells can be measured directly with an ultramicroscopic electrode consisting of a thin glass tube drawn out to a very fine tip (less than 0 5μ) and filled with a solution of potassium chloride The potential difference recorded when the electrode is inserted into the cell amounts to about 5 mV This potential is due to a difference between the concentration of ions (mainly Na and K) inside and outside of the cell so that the inside of the cell is negative (−) in relation to the outside (+) As a wave of excitation passes over the fiber an action potential is recorded in which the potential rapidly approaches zero and overshoots (reversed polarity of the membrane) The resting potential is restored gradually at first and then very rapidly during the later stages of the repolarization process

Electrocardiographic Interpretation Changes in Configuration of the Complexes

The configuration of recorded waves is altered by differences in the rate or sequence of excitation or repolarization during the inscription Certain characteristic changes observed on electrocardiograms are frequently associated with specific abnormal functional states of the myocardium (e g , myocardial ischemia, myocardial infarction and the effects of varying electrolyte concentrations and drugs) The altered electrical activity of the heart under these conditions can be assessed by two very different approaches (*a*) empirically or (*b*) by theoretical analysis Empirical interpretation involves matching certain types of electrocardiographic patterns with specific disease states Such correlations require considerable experience since they involve learning and applying a vast quantity of detailed information collected over the years Comprehensive coverage of this material cannot be achieved in a text of this scope Instead, the theory underlying the production, distribution and recording of potentials from the heart is used to describe factors which may affect the form of electrocardiographic complexes

THE SOURCE OF CARDIAC POTENTIALS

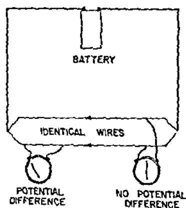
The changes in potentials, recorded as electrocardiograms, resemble electrical phenomena occurring in other excitable tissues such as skeletal muscle, smooth muscle and nerves (see Chapter 7) In the resting state there is a difference in potential between the inside and the outside of these cells This potential difference can be detected only by inserting a microelectrode into individual muscle fibers (Fig 1) The difference in potential between the inside and the outside of a resting myocardial fiber ranges around 75 mV [1, 2] Its presence has been ascribed to a charged cell "membrane "

The Origin of Membrane Potentials

The cell membrane serves as a semipermeable barrier between two very different solutions Outside the cell, the concentration of sodium is very high while the potassium level is very low Within the normal resting cell, potassium is the predominant cation and the sodium concentration is very small To attain a low concentration of sodium within the cells, sodium ions must be selectively transferred from regions of low concentration across the cell membrane to the extracellular spaces where the concentration is high Since active transfer of Na^+ requires movement of a charged particle against a concentration gradient, energy must be expended by oxidative metabolic processes of the cell As Na^+ is removed from the cell, a potential difference develops across the cell membrane which drives K^+ into the cell until its outward diffusion pressure is balanced by the electrical potential Thus, the only requirement for the development of a resting potential across a cell membrane is the selective transfer of sodium ions out of the cell

POTENTIALS IN VOLUME CONDUCTORS

A. POTENTIALS ALONG WIRES



B. POTENTIALS IN A VOLUME CONDUCTOR

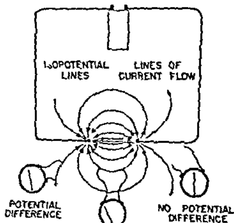


FIGURE 3. *A* Differences in potential can be recorded along a current pathway as in a wire. Indeed the potential difference is the cause of current flow. No potential is recorded from corresponding points on two identical wires and no current flows between these two points.
B Potential differences can be recorded along the lines of current flow in volume conductors. No potential difference can be recorded along lines which are perpendicular to the lines of current flow (see *A* above). The dotted lines indicate isopotential lines along which no potential difference can be recorded.

current source. The potentials diminish with the square of the distance, schematically illustrated by the greater separation of isopotential lines in Figure 4. At a great distance from the current source the potential may be nearly zero so an electrode placed in such a region can be used as a zero reference (indifferent electrode). Since the potential actually becomes zero at an infinite distance the indifferent electrode must be at a point where the potentials are too small to be significant. Whether a potential is significant depends upon the accuracy required of the measurements. If an indifferent electrode is connected to one side of a galvanometer, the electrode on the other side can be used as an exploring electrode to measure the potentials in any portion of the volume conductor. Measurement of potentials with an exploring and an indifferent electrode (termed unipolar recording) is simpler to visualize and to illustrate than bipolar recording in which both electrodes are in regions of high current density (e.g. the standard limb electrodes in routine electrocardiography).

DIPOLES. The difference in potential on the two sides of a membrane can be represented by a positive charge (+) outside the membrane balanced by an equal negative

UNIPOLAR ELECTRODE

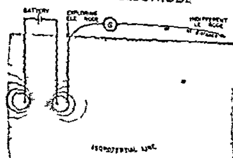


FIGURE 4. A galvanometer records the difference in potential between two points. If absolute potential is to be measured, one side of the galvanometer must be connected to an electrode at zero potential. The potentials in a volume conductor diminish with the square of the distance from a current source as indicated by the progressively increasing separation between isopotential lines. If one of the electrodes is placed at a sufficient distance in the volume conductor the potentials become negligible for practical purposes. Using this distant (indifferent) electrode as a zero reference the exploring electrode can be used to determine the absolute potentials at any point in the volume conductor. This process is called unipolar recording since only one electrode is affected by the potentials.

resolved by considering the principles underlying the recording of external potentials from masses of myocardial tissue rather than from single cells

The Electrical Manifestations of Polarized Membranes

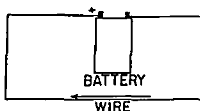
The changes in the concentrations of Na^+ and K^+ cannot be directly measured during the passage of an action potential However, the changes in potential caused by the movements of these charged particles can be amplified, recorded and studied Thus, it is important to consider the electrical manifestations of the distribution of charged particles To this end, it is necessary to be familiar with a few definitions

The fundamental quantities in electricity are positive and negative *charges*, which are equal in magnitude and mutually attract each other Electrical currents are defined in terms of the number of unit charges passing a cross-section of conducting medium each second *Current density* refers to the number of charges passing through a unit area each second Electrical *potentials* are actually differences in potential between two specific points (e g , electrode positions) The *potential difference* between two points is defined as the work necessary to carry a unit positive charge between these two points

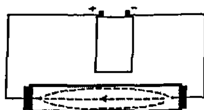
Potential differences and current flow in biologic systems occur in volume conductors instead of wires A *volume conductor* is a medium such as a large vessel containing an electrolytic solution (Fig 2) which conducts electricity in three dimensions Since all the body fluids contain electrolytes the body is a volume conductor Electrical currents flowing through volume conductors may traverse an infinite number of pathways (Fig 2) If the solution is homogeneous the current density is greatest along a direct path between the electrodes Potential differences can be recorded between any two points along a current pathway, either on a wire or in a volume conductor (Fig 3) On the other hand, if recording electrodes are placed at appropriate points on two comparable current pathways, no potential difference is present The current flow progressively diminishes through the portions of the volume conductor at greater distances from the

CURRENT FLOW IN VOLUME CONDUCTORS

A CURRENT FLOW IN WIRE



B CURRENT FLOW IN SALINE



C CURRENT FLOW IN VOLUME CONDUCTOR

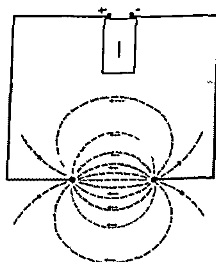


FIGURE 2 *A* Electrical current in a wire is carried by electrons which travel from the negative to the positive terminals of a battery

B Electrical currents are carried through solutions by positive and negative ions which move in opposite directions through liquid media

C A volume conductor is a medium through which electrical current can flow in three dimensions as in a large volume of an electrolyte solution Current density is greatest on a line directly connecting the two electrodes and diminishes along the more circuitous routes

(M_1 and M_2) illustrated in Figure 5*E* subtend the same solid angle and, individually, each would produce the same potential at electrode E The basic mechanism by which two membranes with the same solid angle produce equal potentials at an exploring electrode is indicated in Figure 5*F* On the other hand the pairs of membranes illustrated in Figure 6*A* subtend the same solid angle but positive charges on one membrane and negative charges on the other face the electrode The potentials from these pairs of membranes counteract each other, and no potential can be recorded by the exploring electrode By the same token no potential can be recorded by an exploring electrode near a cell which is polarized equally over its entire surface (Fig 6*B*)

This principle is basic to electrocardiographic interpretation because it applies equally to collections of cells such as the heart During the intervals when the myocardium is completely polarized (between T and P waves) or uniformly depolarized (S-T interval) no potentials are recorded by external electrodes and the galvanometer remains at the baseline Electrocardiographic complexes are inscribed only when part of the myocardium is polarized and the remainder is depolarized (e g during excitation or return to the resting state)

When an area on a cell is depolarized the charges on the membrane are reduced in

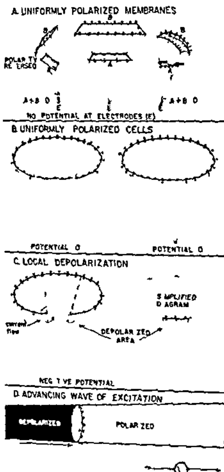


FIGURE 6 *A* The potentials from pairs of uniformly polarized membranes will cancel if they present the same solid angles and the orientation of the charges is reversed In each of the three examples the potential at the electrode is *zero* because the negati e charges of one membrane are precisely balanced by the positive charges of its mate

B If a uniformly polarized cell is considered in three segments the principle illustrated in Figure 6 *A* appl es. In each of the three solid angles the proximal portion of the membrane has positive charges facing the electrode and the more distant portion has negative charges facing the electrode Since the near and distant portions of the membrane subtend the same sol d angle and the charges are oriented in opposite directions their effects cancel and the potential at the electrode is zero Thus a un formly polarized (or uniformly *depolarized*) cell produces no potential wh ch can be recorded by an external electrode In other words f the membrane is uniformly polarized there is no potential difference and no flow of electrical current, and no potential can be recorded

C When a region of a polarized cell becomes partially or completely depolarized electrical currents flow from the polarized regions into the depolarized zone A potential can then be recorded by a d stant electrode the magnitude of the potential is determined by the solid angle subtended by the depolarized area On the far side of the cell, negative charges are not balanced by opposite charges in the depolarized region so the electrode records a negative potential. On the right a suitably charged membrane conforming to the depolarized area is comparable to the more complicated picture on the left, since the solid angle is the same

D The advancing wave of excitation can be visualized as though a suitably charged membrane were placed at the junction between polarized and depolarized *regions* (as in *C* above) Since the outside of the polarized area is positive in relation to the inside an electrode records a positive potential when a wave of excitation advances toward it and a negative potential when a wave of excitation is moving awa

charge (−) on the inside (Fig 1) Each pair of positive and negative charges is called a dipole (Fig 5*A*) The potential produced by a single dipole is insignificant, but in biologic systems, many pairs of positive and negative charges are arranged on opposite sides of membranes

MEMBRANE POTENTIALS When a membrane has positive and negative charges arranged symmetrically as a double layer on opposite sides, it is said to be "polarized" (Fig 5*B*) A large number of charges symmetrically arranged on a membrane combine to produce a potential which can be recorded at some distance A positive potential will be recorded whenever the electrode is closer to the positive than to the negative charges In other words, when the positive charges on a membrane face the exploring electrode, a positive potential is recorded by that electrode Assuming that the number of charges per unit area (charge density) is constant, the magnitude of the recorded potential will be determined by three factors (*a*) the area of the membrane (total number of charges), (*b*) the orientation of the membrane with respect to the electrode and (*c*) the proximity of the electrode to the membrane These three variables can be most easily described in terms of the solid angle subtended by the charged membrane (see Fig 5*C*) The solid angle is greater when the area of the polarized membrane is increased or the radius is diminished according to the formula Solid angle = Area/Radius^2 (Fig 5*C*) The solid angle is maximal when a flat membrane is oriented perpendicular to a line drawn from its center to the electrode (Fig 5*D*) If the membrane is tilted from this position the solid angle is diminished as is the potential recorded by the electrode No potential is recorded when the distances from the electrode to the positive and negative charges are precisely equal (Fig 5*D*)

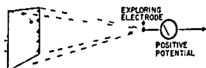
By means of solid angles the relative magnitude and sign of potentials from polarized membranes of any size shape orientation or distance from the electrode can be predicted For example, the two membranes

POLARIZED MEMBRANES

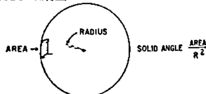
A DIPOLE



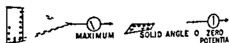
B POLARIZED MEMBRANE



C SOLID ANGLE



D ORIENTATION OF MEMBRANE



E SIZE AND SHAPE OF MEMBRANES

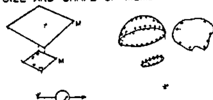


FIGURE 5 *A* A dipole consists of a positive and a negative charge on opposite sides of a membrane
B A membrane with dipoles arranged so that the positive charges are on one surface and negative charges are on the opposite side is called a polarized membrane A potential from a polarized membrane in a volume conductor can be recorded on a distant electrode A positive potential is recorded if the positive charges on the membrane face the electrode The magnitude of the potential depends upon the solid angle subtended by the polarized membrane
C A solid angle actually refers to the apparent size of a surface as viewed from a specific position (e g the site of an electrode)
D When a polarized membrane is perpendicular to a line drawn through its center to the electrode it has maximum apparent size when viewed from the electrode position and it produces its maximal potential in this orientation No potential is recorded from a polarized membrane if only its edge is presented to the electrode because the distance from the electrode to the positive and negative charges of each dipole is exactly equal
E The potential recorded from a charge decreases with the square of the distance but the number of charges on a uniformly charged membrane increases with the square of the distance Thus if M_2 is twice as far from the electrode as M_1 the potential recorded from each charge on M_2 is one-quarter as great but there are four times as many charges as on M_1 Thus each of these two membranes would develop the same potential at the electrode So long as polarized membranes subtend the same solid angle they produce equal potentials at the electrode re-

(e g between polarized and depolarized regions) This is the essence of electrocardiography

RECORDING POTENTIALS FROM THE HEART

Unipolar Recording Potentials from the Heart

The discussion thus far has dealt with potentials recorded from an exploring electrode placed near the source of the electrical activity Unipolar electrodes can be used only if the indifferent electrode is essentially unaffected by the electrical activity (Fig 4) Electrocardiograms can be recorded from the extremities so an electrode placed on them is not sufficiently distant from the heart to be truly indifferent With the body immersed in a large tank of salt water the indifferent electrode can be placed at a great distance from the heart[5] but this is impractical However if wires from three electrodes equidistant from each other and from the heart are joined at a single terminal the potentials developed at the electrodes tend to cancel each other (Fig 7) This principle has been utilized in the central terminal of Wilson[6,7] and provides an acceptable indifferent electrode for unipolar recording

Wilson s central terminal is connected to one side of the galvanometer and an exploring electrode to the other (Fig 7) If the exploring electrode were placed on the surface of the body at the right shoulder (V_R) left shoulder (V_L) and left leg (V_F) the wave of excitation passing through the heart could be viewed from different angles (Figs 8 and 9) These electrode positions are called the unipolar limb leads and can be employed to illustrate the potentials developing during cardiac excitation and recovery

Atrial Excitation and Repolarization

The wave of excitation normally spreads as a concentric ring from its origin at the sino-atrial node As atrial depolarization spreads the area of the excitatory wave first increases and then diminishes Viewed from an electrode facing the apex (left leg) the advancing ring of excitation has positive charges facing the recording electrode, and the recorded P wave is an upward deflection (Fig 8) A negative potential is recorded from the electrode at the right shoulder because the wave of excitation is moving away from this point The wave of excitation travels toward the left shoulder at first, and during the last stages it may pass beyond this position producing first a positive, then a negative (diphasic) deflection (Fig 8)

The wave of repolarization normally follows the same course as the wave of excitation but the polarity is reversed The myocardial fibers in advance of the wave of depolarization are relatively negative (the outside is negative in relation to the inside of the cell) and the repolarized tissue is relatively positive This condition is the reverse of that existing during depolarization and can be represented by a charged membrane with negative charges oriented in the direction of the wave s movement Thus the wave of repolarization (T_a wave) causes a deflection in the opposite direction to that

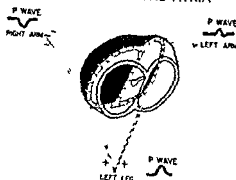


FIGURE 8 As a wave of excitation spreads concentrically through the atrial musculature different patterns are recorded by unipolar electrodes placed on the extremities For example the wave of excitation is advancing toward the left leg which therefore responds to the positive charges facing this electrode and inscribes an upward deflection (see Fig 6D) In contrast the wave of excitation moves away from the right shoulder so a downward deflection is recorded from the right arm If the wave of excitation first advances toward the left shoulder and then recedes from this position a diphasic deflection is recorded from a unipolar electrode on the left arm In each case the magnitude of the deflection at any instant is determined by the solid angle subtended by the wave of excitation as viewed from the effective electrode position (right and left shoulders and symphysis pubis)

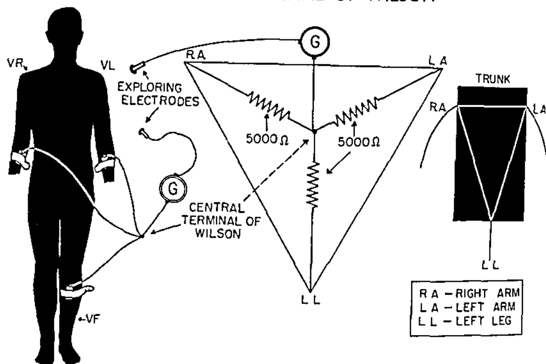


FIGURE 7 Accurate unipolar recording of cardiac potentials requires an indifferent electrode which is unaffected by potentials developed by the heart If electrodes on all three extremity leads are connected through 5000 ohm resistors to a single terminal (the central terminal of Wilson) the potentials at the extremities almost completely cancel out to provide a fairly reliable indifferent electrode The heart is not exactly equidistant from each electrode since it is situated toward one end of a roughly rectangular volume conductor but the resulting errors have not proved too serious for practical purposes

number or reversed in sign and a potential can then be recorded In the region outlined by the solid angle in Figure 6C, a portion of the membrane facing the electrode is illustrated as completely depolarized and the portion of the membrane immediately behind has negative charges facing the electrode *Current flows from the surrounding* polarized membrane into the depolarized zone and, as soon as current flows a potential can be recorded at the electrode Under these conditions the electrode records a negative potential with a magnitude proportional to the solid angle drawn to the junction of the polarized and depolarized areas (Fig 6C) This rather complicated picture can be simplified schematically by substituting a suitably charged membrane conforming to the zone of transition between the polarized and the depolarized membrane Such a hypothetical membrane precisely reproduces *the electrical effects illustrated in the more* complicated drawing Thus a wave of excitation produces a negative potential when it is moving away from an electrode and a positive potential when it approaches an electrode (Fig 6D) In the same way, a wave of excitation passing through a mass of myocardial tissue can be outlined by a solid angle which *indicates the relative magnitude* and sign of a potential recorded from an electrode at a specific site in relation to the electrical disturbance

In summary, myocardial cells produce no external potentials so long as they are either completely polarized or completely depolarized because the equal and opposite charges in each fiber precisely counteract each other Potentials are recorded only from a transition zone between the polarized and depolarized regions where the charged surfaces are not cancelled Stated another way, potentials can be recorded only when electrical current *flows in response to potential differences*

of the P wave (see Fig 2 Chapter 14) The T_a wave has longer duration and smaller amplitude than the P wave because repolarization is a slower process It is generally obscured by the QRS complex which normally occurs during inscription of the T_a wave

Ventricular Excitation and Repolarization

As the wave of excitation passes down the conduction system the solid angle subtended by this bundle of tissue is very small and the resultant potentials are not sufficient to produce a deflection The first recorded potential develops when a significant area of ventricular myocardium has been invaded by a wave of excitation The configuration of the QRS complex will depend upon the sequence of ventricular excitation and the direction taken by the excitatory waves

THE QRS COMPLEX. Ventricular excitation can be schematically illustrated by a simplified diagram as in Figure 9 The magnitude and sign of the potentials are indicated by solid angles subtended by the margins of the transitional zone between the polarized and depolarized regions The wave of excitation travels toward the left leg (V_F) producing a positive deflection and moves away from the right shoulder as indicated by the negative deflection at V_R The small solid angle subtended at V_L is associated with a small deflection which may be upward or downward depending upon the exact orientation of the spreading wave In Figure 9 the largest deflections during the entire course of depolarization occur in V_R and V_F since the solid angles from these electrode positions are greater than that from V_L The patterns derived from V_L are very susceptible to variations in the orientation of the heart They are generally diphasic the downward deflection predominates when the heart is oriented more vertically and the upward deflection is more prominent if the long axis of the heart approaches horizontal

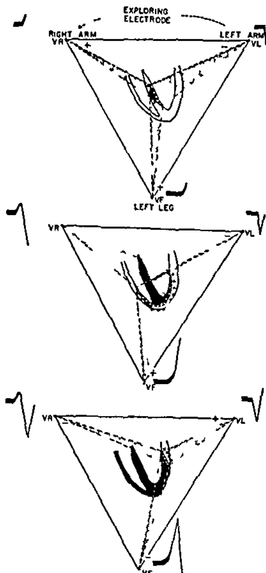
THE S-T SEGMENT When ventricular excitation is complete the degree of membrane polarization is normally uniform throughout the myocardium (Fig 9B) Under these conditions no potentials are recorded by external electrodes (see Fig 6B) and the galvanometer returns to the baseline where it remains until the effects of repolarization are manifest in the inscription of the T wave

THE T WAVE. The normal sequence of ventricular repolarization is unknown Since a wave of repolarization should produce potentials opposite in sign from those developed during depolarization, the QRS and T waves would deflect in opposite directions if these two processes followed the same course On the contrary, the QRS and T waves usually deflect in the same direction so the process of repolarization does not follow the same sequence as depolarization Experimentally repolarization can be delayed by applying pressure to the myocardium Repolarization may be delayed in the subendocardial layers of myocardium owing to high intraventricular pressure affecting the inner layers more than the external layers On this basis, repolarization is frequently visualized as beginning in the outer layers of myocardium and progressing toward the endocardial surface, in general retracing the path of the wave of excitation This traditional view will be followed in the present discussion although it has not been adequately established by direct experimental evidence The T waves are generally of smaller amplitude and longer duration and have a more rounded contour than the QRS complex because repolarization is a slower process than depolarization The delay in repolarization is illustrated in the monophasic action potential from a single myocardial fiber (Fig 1) in which the upward deflection (depolarization) occurs much more rapidly than the return to the baseline (repolarization) A schematic representation of the inscription of a T wave from unipolar extremity electrodes is illustrated in Figure 9C

With simplified diagrams as in Figure 9 it is possible to illustrate a mechanism by which ventricular excitation can produce reasonable facsimiles of the deflections recorded from unipolar limb leads Com-

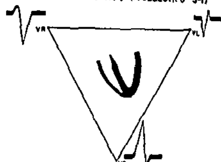
VENTRICULAR EXCITATION

A. VENTRICULAR DEPOLARIZATION (QRS)



VENTRICULAR RECOVERY

B. UNIFORM DEPOLARIZATION (ISOELECTRIC S-T)



C. REPOLARIZATION (T WAVE)

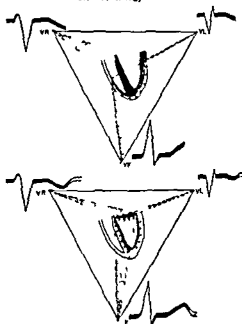


FIGURE 9 *A* The origin of the potentials recorded by unipolar extremity electrodes during ventricular depolarization is illustrated schematically The initial wave of excitation is presented as originating on the left side of the interventricular septum and moving toward the right ventricle This area of excitation would produce an upward deflection in both V_R and V_F because the positive charges face these electrodes A downward deflection would be recorded from V_L because the wave of excitation is moving away from the left shoulder

At a later stage the wave of excitation conforms roughly to a cuplike shell of excitation progressing from endocardium to epicardium Since the wave of excitation is moving toward V_F and away from V_R the deflections in these two leads are in opposite directions

If a wave of excitation invades the basilar portion of the left ventricular wall in the final stages it is moving toward the left shoulder A downward deflection is inscribed from V_R and V_F and an upward deflection from V_L

B When the ventricles are uniformly depolarized no potentials are recorded from any of the external electrodes (see Fig 6*B*)

C Since depolarized regions are negative with respect to polarized myocardium a negative deflection is recorded when a wave of repolarization advances toward an electrode Assuming that repolarization begins on the epicardial surface of the ventricles and progresses inward a negative deflection would be recorded at V_R since the activity is moving toward the right shoulder A positive deflection would be recorded at V_F and in the example illustrated very little potential would be recorded by V_L because a very small solid angle would be subtended

The endocardial region of the left ventricle may be the last portion to be repolarized Here as in the other examples the cuplike configuration of the wave of excitation can be represented by a flat polarized membrane at the junction between polarized and depolarized myocardium at the base of the heart (see Fig 6*C*)

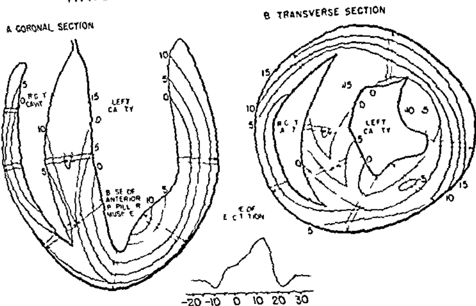


FIGURE 11 The normal sequence of activation within the ventricles is illustrated on a coronal and a transverse section of a dog's heart. The position of the electrodes used to gather the data is indicated. Successive positions of the wavefront are indicated by lines joining corresponding levels on the electrodes. Each of these is labelled with the time before or after the fixed time-reference potential. General features of excitation are described in the text.

mately correct. We have recorded potentials occurring between the end of P and the initial ventricular deflection in the vicinity of the A-V node and from the branches of the bundle within the ventricle. The impulse reaches the left ventricular myocardium nearly simultaneously in two places: one where the posterior division of the left bundle branches arrives at the junction of the posterior free wall and septum approximately midway between apex and base, the other where the anterior branch of the left bundle reaches the intersection of wall and septum in the mid anterior region. Slightly later activity commences in the right ventricle at the termination of the bundle on that side near the anterior papillary muscle. Activation of the septal endocardial surfaces takes place at about 1 m. per second in the lower regions, but the endocardium of the free walls is activated very rapidly owing to extensive endocardial branching of the Purkinje net. Therefore excitation is nearly simultaneous at many points. Under the papillary muscles, however, the earliest points are most often between endocardium and epicardium as if the rapidly conducting endocardial layer had extended through from either side. Otherwise there is no intramural penetration of the Purkinje fibers into the ventricular walls. The latest endocardial points excited in our studies thus far are in the basilar portions of the septum and free walls.

The wave of excitation travels at about 0.3 m. per second through the ventricular walls and septum. In the walls this movement is directed epicardially. In the septum excitation proceeds from both surfaces toward the center of the muscle (Figs. 11 and 12).

As a simple summary, we may say that the excitation consists of three phases: the first from left to right in the septum, the second from endocardium to epicardium in the mid and apical free walls (with activity proceeding centripetally from both septal

plexes with precisely the same shape could be produced by many different sequences of ventricular excitation The only way to determine the exact course of the spreading waves of excitation is to measure their arrival at electrodes inserted into the ventricular walls In recent years, studies of this type have produced conflicting results [8–10] Since this question is a basic issue in electrocardiography, it deserves particular attention The sequence of ventricular excitation has been most carefully investigated by a group working with Dr Allen Scher, who kindly agreed to summarize his views on this subject

Excitation of Canine Ventricles (*by Allen M Scher*)

During the past several years, we have been investigating the normal spread of excitation through the ventricles of the dog The most important equipment used in the study has been the multipolar electrode constructed of 15 fine tungsten wires around a central shaft with tips staggered at close (1 0 mm or 0 5 mm) intervals (Fig 10) This electrode may be inserted into the right or left wall of the heart or it may be pushed through the right wall and cavity into and across the interventricular septum Records have been taken from these sites as well as from the vicinity of the A-V node and from buried portions of the conducting system

The recording system used in conjunction with this electrode consists of a 16-tube cathode ray oscilloscope which permits simultaneous recording from (*a*) all points on the electrode as well as (*b*) a fixed time reference potential and (*c*) a conventional electrocardiogram A switching system permits recording of a unipolar potential (each *terminal against an indifferent electrode*) or bipolar potentials (difference between adjacent terminals)

In the initial studies we concentrated on the mechanism of ventricular activation Recent years had seen classic concepts of ventricular activation challenged The function and even the existence of the Purkinje tissue had been denied It had been claimed that excitation was carried within the muscle bundles, or that the direction of the fibers determined the speed of activation Our initial studies supplied facts to confirm and extend Lewis' hypotheses concerning the mechanisms of ventricular depolarization [11] Later studies, which are still under way, utilize extrasystoles, bundle-cutting and detailed recording throughout many hearts in delineating the course of normal excitation and the factors responsible for it The following summarizes some findings to date

The traditional picture of the Purkinje function in ventricular excitation is approxi

RECORDING POTENTIALS WITHIN VENTRICULAR WALLS

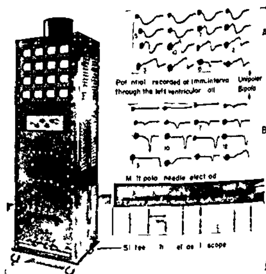
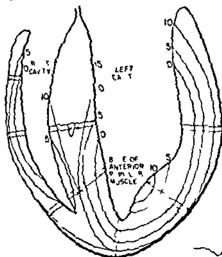
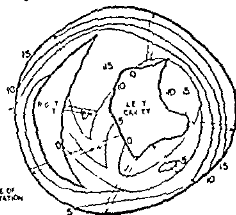


FIGURE 10 A multipolar electrode is illustrated at the bottom on the right Small bubbles have been formed at the tip of each electrode by electrolysis The 16-channel oscilloscope is shown at the left *A* and *B* show unipolar and bipolar records taken with this equipment from electrodes inserted through the left ventricular wall The upper set of unipolar records (*A*) shows cavity potentials on channels 1 to 4 channel 14 was at the ventricular surface Progression of the wave of excitation through the wall is indicated on channels 5 through 13 The bipolar records show the difference in potential between adjacent unipolar electrodes In other words channel 1 of the bipolar leads shows the difference between the first two unipolar electrodes The recording convention provides a downward deflection if the endocardial terminal of a bipolar lead is excited first As can be seen excitation proceeds from inside out along this electrode In both unipolar and bipolar records a fixed time reference potential appears on channel 15 and a lead II electrocardiogram is presented on channel 16

WAVE OF EXCITATION IN DOG VENTRICLE





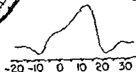


FIGURE 11 The normal sequence of activation within the ventricles is illustrated on a coronal and a transverse section of a dog's heart. The position of the electrodes used to gather the data is indicated. Successive positions of the wavefront are indicated by lines joining corresponding levels on the electrodes. Each of these is labelled with the time before or after the fixed time-reference potential. General features of excitation are described in the text

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RECORDING POTENTIALS WITHIN VENTRICULAR WALLS

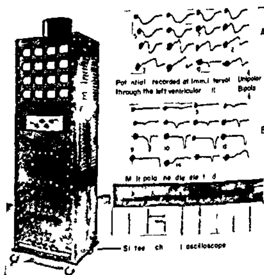


FIGURE 10. A multipolar electrode is illustrated at the bottom on the right. Small bubbles have been formed at the tip of each electrode by electrolysis. The 16-channel oscilloscope is shown at the left. *A* and *B* show unipolar and bipolar records taken with this equipment from electrodes inserted through the left ventricular wall. The upper set of unipolar records (*A*) shows cavity potentials on channels 1 to 4; channel 14 was at the ventricular surface. Progression of the wave of excitation through the wall is indicated on channels 5 through 13. The bipolar records show the difference in potential between adjacent unipolar electrodes. In other words, channel 1 of the bipolar leads shows the difference between the first two unipolar electrodes. The recording convention provides a downward deflection if the endocardial terminal of a bipolar lead is excited first. As can be seen, excitation proceeds from inside out along this electrode. In both unipolar and bipolar records, a fixed time reference potential appears on channel 15 and a lead II electrocardiogram is presented on channel 16.

(e g, lead I and lead III) The method requires use of the Einthoven triangle which is based on the concept that the heart lies in a large, uniform volume conductor at the center of an equilateral triangle with the limb electrodes at the apices In spite of the rectangular configuration of the trunk (Fig 7) and the lack of homogeneity of the body, these assumptions are more completely real ized than would appear at first glance[5] The positive and negative signs on Einthoven s trian le (Figs 13 14) indicate that the limb electrodes are connected to the recording galvanometer in such a way that an upward deflection is recorded under the following conditions in each lead

- *Lead I* When the left arm is positive in relation to the right arm
- *Lead II* When the left leg is positive in relation to the right arm
- *Lead III* When the left leg is positive in relation to the left arm

The method of determining an instantaneous electrical axis at a particular moment in time is illustrated in Figure 14 The instantaneous axis indicates the mean direction in which the wave of excitation is traveling at a particular instant and its length represents the relative magnitude of the externally recorded potentials developed at that time (Fig 14*B*) If instantaneous electrical axes are determined at short intervals during the remainder of ventricular excitation, the series of instantaneous vectors change in length and orientation during the cardiac cycle (Fig 14*C*) A series of instantaneous electrical axes constitutes a *vectorcardiogram*

Vectorcardiograms A line connecting the points of the instantaneous vectors describes a loop Loops of this type can be inscribed on the face of a cathode ray oscilloscope, thus continuously indicating the instantaneous electrical axis from moment to moment[13] The instantaneous electrical axes illustrated in Figure 14C actually represent three-dimensional vectors as projected on a frontal plane Since the original potentials actually

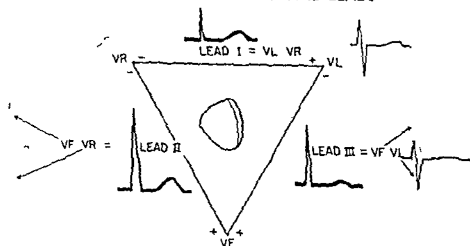
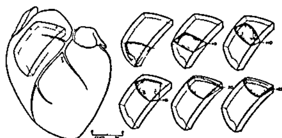


FIGURE 13 Each standard *limb lead* represents the difference in potential between two extremities Since the unipolar limb leads record the potentials at the individual extremities subtracting the potentials recorded at the right arm (V_R) from the potentials at the left arm (V_L) should produce the patterns recorded from lead I The process is more easily visuali ed in deriving lead II complexes by subtracting V_R (dashed li e) from V_F (d tted line) An upward deflection is inscribed in lead II when V_F is positive with respect to V_R (note positi e and negative signs on the Einthoven triangle) This schematic drawing indicates the complex origin of the standard limb leads as compared to the unipolar extremity leads

WAVE OF EXCITATION IN VENTRICULAR WALLS

A RIGHT VENTRICULAR WALL



B LEFT VENTRICULAR WALL

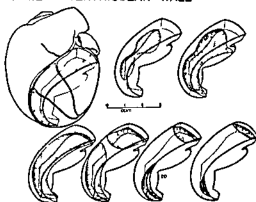


FIGURE 12 *A* A portion of the anterior right ventricular wall was studied with 15 multipolar electrode insertions indicated by the small dots Planes have been drawn to connect points simultaneously excited These delineate successive positions of the activating wavefront at 5 msec intervals after the time reference

B A portion of the anterior left ventricular wall is represented in the manner described in *A*

endocardial surfaces), the third phase is movement toward the base of the walls and septum

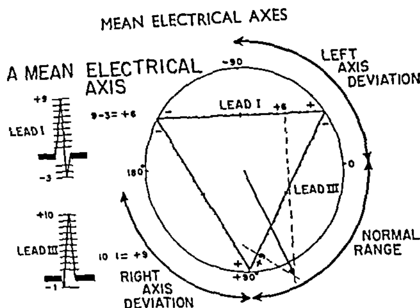
TYPES OF ELECTROCARDIOGRAPHIC LEADS

The Characteristics of Standard Limb Leads

When electrodes are applied to two extremities and connected to a galvanometer the records indicate continuously the difference in potential between the two electrode positions The standard limb leads can be recorded by measuring the potential difference between each pair of unipolar records, as in Figure 13 In accordance with the polarity indicated on Einthoven s triangle (+ and − signs), the complex at the negative end of the lead line is subtracted from the complex at the positive end It is apparent that the standard limb leads are more complicated than unipolar leads, since the potentials fluctuate at both electrodes and the final record represents the difference in potential at each instant in time Because it is difficult to visualize the result of subtracting one solid angle from another, this method is not widely used to describe the origin of the potentials recorded on standard limb leads Instead an electrical axis is usually employed for this purpose

THE ELECTRICAL AXIS OF THE HEART Although the amplitude and polarity of potentials recorded from unipolar electrodes can be predicted by knowing the solid angle subtended by an area of uniform charge density, the process cannot be reversed In other words, the portions of the heart undergoing depolarization cannot be determined from externally recorded potentials such as the electrocardiogram Areas of depolarization in an infinite variety of combinations can theoretically produce the electrocardiographic pattern recorded from any particular electrode position For this reason, electrical activity in the heart is often represented by vectors which indicate the magnitude and mean direction of excitation without specifying the location of the activity An arrow can be erected in the center of an area of spreading activity (see Fig 14*C*) to indicate the mean direction of progression (the mean orientation of the charges) with the length of the arrow proportional to the solid angle (the magnitude of the recorded potential) Vectors can be derived from the electrocardiographic records obtained with the standard limb leads Such vectors indicate the mean direction and magnitude of potentials developed within the heart as projected upon a frontal plane However, they do not identify the specific regions of the heart being invaded by waves of excitation

Instantaneous electrical axes An electrical axis or vector can be determined for any instant during the cardiac cycle from simultaneously recorded standard limb leads



B MEAN SPATIAL AXIS

VERTICAL ORIENTATION | AVERAGE ORIENTATION | HORIZONTAL ORIENTATION







CLOCKWISE ROTATION | COUNTER-CLOCKWISE ROTATION

Electrical axis ——○

Anatomic axis - - - ➤

FIGURE 15-4 *A* The mean electrical axis is computed from two of the three standard limb leads (e g leads I and III) The sum of the downward deflections is subtracted from the sum of the upward deflections For example the vertical height of the R wave above the baseline is measured in millimeters (+9 mm. in lead I) The total amplitude of the downward deflections (−3 mm. in lead I) is added algebraically to the height of the R wave (+9) and leaves a net value of +6 At a point 6 units toward the plus sign on the lead I line of the triangle a perpendicular is erected The net amplitude of upward and downward deflections in lead III is +9 (+10 − 1) A perpendicular erected 9 units toward the plus sign on lead III is extended to intersect the perpendicular from lead I An arrow drawn from the center of the triangle to the intersection of these two perpendicular lines is the *mean electrical axis*

B The mean electrical axis oriented in three dimensions (spatial vector) is directed rather strongly posteriorly For this reason rotation of the heart around a longitudinal axis produces large changes in the orientation of the mean electrical axis as projected on a frontal plane This is the principal mechanism by which changes in the orientation of the heart produce changes in both the mean electrical axis and the configuration of patterns from the various electrocardiographic leads

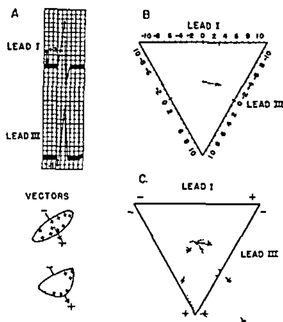


FIGURE 14 *A* An instantaneous electrical axis can be derived from two standard limb leads recorded simultaneously Simultaneous points on the two complexes are selected (e g 0 02 second after the beginning of the QRS complex) At this instant the galvanometer had deflected upward 3 mm in lead I

B From a point +3 units on the lead I line of Einthoven s triangle a perpendicular line is erected Similarly at this same instant the deflection was 1 mm below the bottom of the baseline in lead III A perpendicular line is erected at −1 unit on the lead III line An arrow drawn from the center of the triangle to the intersection of the perpendicular lines *is the instantaneous electrical axis*

C Such vectors indicate the mean direction in which the wave of excitation is advancing at a particular instant If vectors are derived at intervals of 0 02 second during the remainder of the QRS complex (black dots on the QRS complexes) a series of instantaneous electrical axes can be derived This series of vectors indicates the changing orientation and magnitude of potentials developing during ventricular excitation and is called a *vectorcardiogram*

develop in three dimensions, a more complete picture of the shifting patterns of potentials can be derived from three-dimensional vectors stereovectorcardiography [14–17]

Although stereovectorcardiography has added little to our basic knowledge of electrocardiography, the graphic representation of vectors helps to visualize the process of ventricular excitation (see Fig 15*B*) An average or mean electrical axis has proved useful in electrocardiographic interpretation even though it is not nearly as accurate or complete as a vectorcardiogram or a series of instantaneous vectors

The mean electrical axis Theoretically a mean electrical axis should be the resultant of instantaneous vectors such as those illustrated in Figure 14*C* The routine method of determining the mean electrical axis is a compromise based on the questionable assumption that the height of the Q R, and S deflections is proportional to the area under them The net upward or downward deflection is determined for the typical QRS complex in two of the three standard leads (e g , leads I and III) As indicated in Figure 15 the mean electrical axis is determined in much the same way as an instantaneous electrical axis (see Fig 14) Note that in Figure 15 the mean electrical axis approximates the resultant of all the instantaneous axes illustrated in Figure 14*C* Although the mean electrical axis is intended to represent the mean value for the instantaneous axes, serious discrepancies often occur, particularly in the presence of ventricular conduction disturbances (see Fig 26)

The direction of the mean electrical axis is expressed in degrees on a circle drawn from the center of the equilateral triangle In most normal subjects the mean electrical axis lies in the range from 0 to +90 degrees (+100 degrees according to some authors) A mean electrical axis greater than +90 degrees is termed right axis deviation, while a shift of the electrical axis into the negative range is called left axis deviation A large downward deflection in lead III and a tall R wave in lead I produces left axis deviation A number of factors influence the orientation of the mean electrical axis, including the position of the heart within the thorax rotation of the ventricles around their longitudinal axis (Fig 15*B*), the thickness of the ventricular walls (e g hypertrophy) and the rate and sequence of ventricular conduction For example, left axis shift occurs when the heart is *horizontally* oriented, as in short stocky individuals with high diaphragms Vertical orientation of the

are farther from the electrodes An electrode in the lower esophagus has a fairly high degree of specificity for certain regions on the posterior aspect of the atria[21] and ventricles -- Small area of myocardial destruction caused by occlusion of coronary arteries may produce characteristic signs at these various electrode positions when no indication appears on records from the more distant standard limb leads Electrocardiographic changes during myocardial infarction are discussed in Chapter 16

The precordial leads are also used to assess the orientation of the heart within the thorax and the presence of ventricular enlargement These applications require an understanding of two characteristics of the precordial electrocardiograms (*a*) the intrinsicoid deflection and (*b*) the transitional zone

INTRINSICOID DEFLECTION If a unipolar exploring electrode is placed directly on the surface of the *right ventricle the* time during which the wave of excitation passes from the endocardial surface *to the epicardial* surface under the electrode can be measured As the wave of excitation moves toward the electrode a positive potential is recorded When the excitatory process breaks through the surface under the electrode the positive potential is suddenly replaced by a negative potential because excitation in other parts of the heart is moving away from this electrode The abrupt transition between increasing positivity and increasing negativity (the peak of the R wave) occurs at the moment the excitatory process breaks through the surface immediately under the electrode and is called the *intrinsic* deflection The interval between the beginning of the QRS complex and the intrinsic deflection (peak of the R wave) is a measure of the time in which the wave of excitation traveled through the myocardial wall lying under the electrode (ventricular activation time) The remainder of the complex represents activation in more distant portions of the ventricular walls The intrinsic deflection occurs earlier in records from the epicardial surface of the right ventricle than in those from the left ventricle Although exploring electrodes cannot be placed directly on the surface of a patient s heart precordial leads record very similar electrocardiographic patterns These leads are often called semi-direct leads and the downward deflection recorded following the peak of the R wave is called the *intrinsicoid* deflection[23]

The routine use of precordial leads includes recording from points overlying the right ventricle (V_1 and V_2 in Fig 16) Complexes from these leads usually have small R waves a short interval between the onset of QRS and the intrinsicoid deflection (e g , 0 0 second) and a deep S wave In lead V_1 the small R wave represents the rapid penetration of the thin walled right ventricle by the wave of excitation and the large S wave indicates the spread of excitation away from the electrode in the more distant portions of the heart (primarily the left ventricle) Precordial leads V_5 and V_6 normally lie over the left ventricle and their records are characterized by large R waves a more delayed intrinsicoid deflection (e g 0 04 second) and a small S wave (Fig 16*C*) This configuration *denotes* that the wave of excitation in the left ventricle advances toward the electrode during a greater proportion of the QRS interval than in the right ventricle presumably because the left ventricular wall is much thicker If the left ventricular wall is abnormally thick ventricular activation time is even more prolonged so the intrinsicoid deflection *tends to* be delayed (0 05 second or longer) In the same manner right ventricular hypertrophy is associated with larger R waves and *a delayed* intrinsicoid deflection (longer than 0 03 second) in the right precordial leads (V_1 and V_2) There is some controversy whether ventricular activation time should be measured from the beginning of the QRS to the peak of the R wave or from the beginning of the R wave to the point at which the downward limb of the R wave crosses the baseline Furthermore accurate measurement of such very brief intervals is difficult For these and other reasons there are wide differences of opinion concerning the value

heart tends to shift the mean electrical axis toward the right (Fig 15*B*) So long as the heart is normal, these axis shifts are generally confined to the normal range More extreme axis deviation may result from predominant enlargement of one ventricle (e g, left ventricular *preponderance produces left axis* deviation)

Unipolar Precordial Leads

The anterior and posterior aspects of the heart can be explored by means of electrodes applied directly to the surface of the thorax (Fig 16) This is important because the limb leads respond primarily to potentials developed on the lateral, superior and inferior regions of the heart Electrical activity on the anterior and posterior surfaces subtends very small solid angles from the limb electrodes and produces relatively small potentials For these reasons, records of cardiac potentials from unipolar electrodes, positioned at specific points on the thoracic wall over the heart, have become a part of the routine electrocardiographic examination [7] The myocardium immediately under these precordial electrodes contributes more to the recorded deflections than do myocardial walls farther away A small area of altered polarization in the proximal zone subtends a relatively large solid angle (see V_4 in Fig 16*A*), and shows up as a large deflection from that particular electrode The central region of the solid angle has the greatest influence on the recorded potentials Around the periphery of the solid angle, the membranes *approximate a radius of the solid* angle and contribute very little to the recorded potentials

Changes in the functional state of small *myocardial areas can be detected by an* electrode placed sufficiently near the defect (e g, local myocardial ischemia) Unfortunately, unipolar electrodes can be placed in close proximity to the myocardium only over the precordium In some cases it is desirable to explore additional areas on the surface of the thorax For example, unipolar electrodes placed on the back provide an appreciable degree of localization over the posterior surface of the heart[20] even though these points

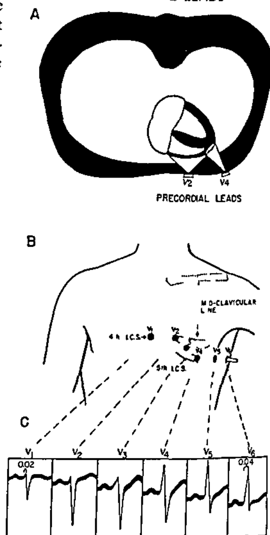


FIGURE 16 *A* Electrodes placed at prescribed positions on the precordium are influenced to a greater extent by the myocardium directly beneath than by more distant regions For this reason they are termed semi-direct precordial leads A local region of depolarization (stippled area) would have a greater effect on V_4 than on V_2 *illustrating* the utilization of these leads for detecting altered potentials from local areas under the electrodes

B Unipolar precordial electrodes are routinely placed on six positions V_1 is in the fourth intercostal space (I C S) at the right sternal edge V_2 is in the fourth I C S just to the left of the sternum V_4 is in the fifth I.C.S in the mid-clavicular line with V_3 midway between V_2 and V_4 On a horizontal line drawn from V_4 V_5 is located at the anterior axillary line and V_6 at the mid axillary line

C Electrocardiographic patterns recorded from the six precordial electrode positions are schematically presented In V_4 the amplitude of R and S are approximately equal This is termed the *transitional zone* which is believed to lie over the interventricular septum

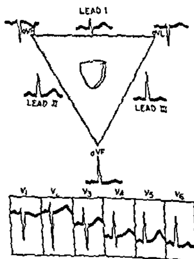
(Fig 17) Currently routine electrocardiography includes records from the three standard limb leads the three unipolar or augmented extremity leads and the six precordial positions (see Fig 19) Many more electrode positions have been advocated but they will not be considered here

THE ELECTROCARDIOGRAPHIC POSITION OF THE HEART

The orientation of the heart within the thorax has important bearing on the interpretation of electrocardiograms just as it influences roentgenographic interpretation (see Chapter 11) For example electrocardiographic patterns which suggest enlargement of the left ventricle can be caused solely from a horizontal orientation of the heart However the electrocardiographic indications of cardiac orientation do not correspond to the anatomic position so we may speak of the electrocardiographic position of the heart For example the mean electrical axis of a horizontal heart may be directed toward the left shoulder This obviously does not imply that the long axis of the heart is rotated until the apex lies above the base of the heart (see Fig 15*B*)

Analysis of the electrical position of the heart has been extended in recent years to include rotation around three axes the anteroposterior the transverse and the longitudinal (see Fig 15*B*) In view of the transitional stages of rotation around any or all of three axes the heart can occupy innumerable electrical positions For example, electrocardiographic patterns of 45 different orientations of the heart have been presented by LaDue and Ashman [27] Such an approach is far too comprehensive for the present discussion Instead examples of electrocardiographic patterns in normal hearts oriented vertically or horizontally are presented

HEART ORIENTATION ON ROUTINE E C G LEADS



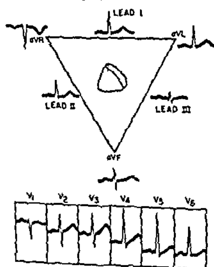
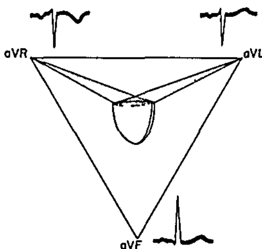


FIGURE 18 *A* When the heart is oriented vertically within the thorax the potentials viewed from the right and left shoulders are similar so the patterns obtained from aV_R and aV_L are also similar The QRS in lead I has low potentials and is diphasic since it represents the difference between aV_R and aV_L (see Fig 13) The transitional zone between V_3 and V_4 indicates a slight shift of the interventricular septum toward the right The intrinsicoid deflections are within normal limits throughout indicating that these changes are not due to ventricular conduction disturbances or hypertrophy

B The horizontal heart has a small diphasic lead *III* which may be slurred or notched The augmented extremity leads are similar to those illustrated in Figure 17 and the V leads show a transitional zone at about V_3 which indicates a counterclockwise rotation of the ventricles around their longitudinal axis (Fig 15*B*)

EFFECTS OF HEART ORIENTATION ON UNIPOLAR LIMB LEADS



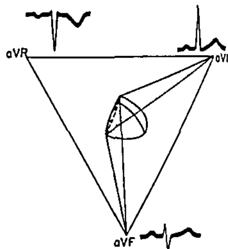


FIGURE 17 *A* When the heart is oriented vertically the QRS complexes are similar in leads aV_R and aV_L
B In the horizontal heart aV_R and aV_L are essentially mirror images a phenomenon which suggests that the wave of excitation actually progresses from right to left This is confirmed by the diphasic QRS in aV_F

of the intrinsicoid deflection in analyzing electrocardiograms

THE TRANSITIONAL ZONE In Figure 16 it should be noted that there is a transition from a large S wave on the right side of the precordium to a large R wave on the left The R and S waves in V_4 have almost equal amplitude The precordial positions at which R and S are equiphasic indicate the transitional zone," and are believed to overlie the interventricular septum [24] If the position of the heart within the thorax changes, the transitional zone tends to shift to one side or the other The precordial localization of the transitional zone is particularly affected by rotation of the ventricles around their longitudinal axis For this reason, the configuration of the QRS complex in the precordial leads is useful in estimating the orientation of the heart within the thorax (*vide infra*)

Augmented Extremity Leads

In 1942, Goldberger[25 26] described a simplified technique for recording electrocardiographic patterns from the extremities Instead of connecting all three extremity leads to a central terminal and positioning an exploring electrode, Goldberger connected two extremity leads to a single terminal and recorded the potential difference between that combination and a third extremity electrode Thus, he achieved a compromise between standard limb leads and unipolar extremity leads Goldberger leads record deflections of greater amplitude than appear from unipolar leads connected to the Wilson terminal and, for this reason, have been called "augmented extremity leads To be more precise, when the Wilson unipolar lead is used the deflection amplitude is a little more than 50 per cent (1 1 72) of that obtained with standard limb leads, while use of augmented extremity leads results in an amplitude about 86 per cent the size of that recorded through standard leads Although the augmented extremity leads are not truly unipolar limb leads, they have been used in much the same way, and are designated aV_R aV_L, and aV_F to distinguish them from the unipolar leads illustrated in Figure 7 A principal advantage to the Goldberger leads is that they can be recorded by adjusting the lead selector switch on standard electrocardiographs and do not require the use of an exploring electrode The augmented extremity leads are frequently used in lieu of the unipolar limb leads for indicating the electrocardiographic position ' of the heart

from patients with apparently similar degrees of ventricular enlargement. Signs of left ventricular hypertrophy appear in the example presented in Figure 19. This is a rather extreme case chosen to show clues which may be useful in recognizing the condition.

In Figure 19 the R wave is tall in lead I and very small in lead III. The very deep S_{III} combined with a tall R_1 is responsible for the deviation of the mean electrical axis to the left beyond the normal range. The QRS interval is less than 0.10 second so the altered QRS configuration is presumably due to hypertrophy rather than to a ventricular conduction disturbance (*vide infra*). The augmented extremity leads (aV_R, aV_L and aV_F) indicate that the electrocardiographic position of the heart is horizontal. In the precordial leads R waves predominate in V_2 through V_6 so the transitional zone has shifted strongly toward the right. In this example the horizontal position of the ventricles is accompanied by marked counterclockwise rotation around the longitudinal axis. The T waves are inverted in leads I, aV_L, V_4, V_5 and V_6; this situation is frequently described as a ventricular "strain" pattern.

LEFT VENTRICULAR STRAIN PATTERNS. The T wave may become flattened or inverted under a wide variety of conditions in which an abnormally severe load is imposed upon a ventricle. If the "strain" is transient the changes in T wave configuration are reversible. In general the T waves tend to deviate in a direction opposite to the main deflection of the QRS complex (e.g., leads I, aV_L, V_4, V_5, V_6 in Fig. 19). The mechanisms which produce changes in the S-T, T complex are not understood but will be considered in relation to abnormalities of repolarization (*vide infra*). The term "strain pattern" has been criticized because it implies that mechanical features of cardiac function are indicated by the electrical activity, which is clearly impossible. No widely acceptable substitute for the term has been offered thus far.

Strain patterns appearing with other clinical and electrocardiographic signs of

FRONTAL VECTORCARDIOGRAM IN LEFT VENTRICULAR HYPERTROPHY

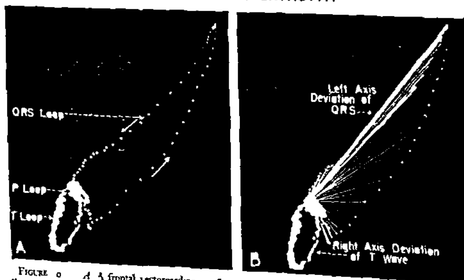


FIGURE 20. *A*. A frontal vectorcardiogram from a patient with extreme left ventricular hypertrophy illustrates the marked deviation of the QRS and T loops.
B. The many instantaneous axes (and *mean* electrical axis) are clearly deviated to the left and upward (left axis deviation beyond the normal range). The rightward deviation of the T wave indicates that the T waves deflect in a direction opposite to the main QRS vectors, a sign of left heart strain.

LEFT VENTRICULAR HYPERTROPHY OF HORIZONTAL HEART

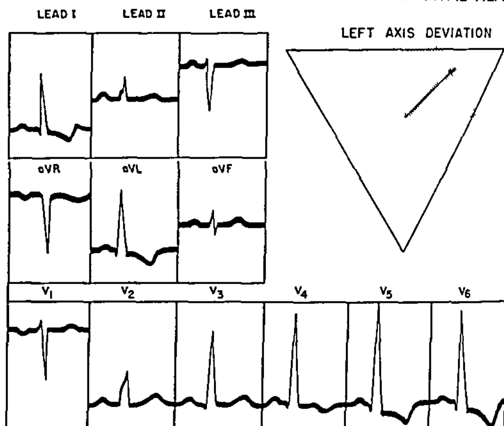


FIGURE 19 Electrocardiographic signs of left ventricular hypertrophy in this patient with a horizontal heart consist of a tall R_I, small R_{III} and deep S_{III}. These changes in the standard limb leads produce deviation of the mean electrical axis to the left beyond the normal range. The presence of a horizontal heart is affirmed by the tall R wave in aV_L and the diphasic deflection in aV_F (see also Fig. 18). The R wave predominates in V_2 through V_6 indicating that the transitional zone has been shifted to the right. The intrinsicoid deflection (peak of R) occurs more than 0.05 second after the beginning of the Q in $V_{5, 6}$. Inversion of T waves and depression of the S-T segment (strain patterns) occur in leads I, aV_L, $V_{4, 5, 6}$. (From a record obtained through the courtesy of Dr. Samuel Aronson.)

(Figs. 17, 18). Goldberger[26] discussed the subject more extensively. The electrical position of the heart must be considered in evaluating electrocardiographic evidence of ventricular enlargement.

ELECTROCARDIOGRAPHIC SIGNS OF CHAMBER ENLARGEMENT

For many years, routine electrocardiographic interpretation was based almost exclusively on the standard limb leads. Ventricular preponderance or hypertrophy was recognized by those changes in QRS configuration which cause the mean electrical axis to deviate beyond the range of normal (see Fig. 15). The basis for these changes in QRS configuration could be convincingly rationalized in accordance with accepted electrocardiographic theory. More recently, the widespread utilization of unipolar precordial and limb leads has greatly broadened the scope of electrocardiographic interpretation to include more complete information concerning the orientation of the heart, the intrinsicoid deflection and changes in the S-T, T complex. The criteria for predominant hypertrophy of each ventricle have become diversified, more empirical and more controversial.

Left Ventricular Hypertrophy

Selecting a "typical" series of electrocardiograms to illustrate left ventricular hypertrophy is extremely difficult because such a wide diversity of records is obtained

basis for attempting to detect left ventricular hypertrophy in the general run of patients A comprehensive list of criteria for this diagnosis used by Sokolow and Lyon [8] is presented in Table 5 Evaluating a given

TABLE 5 THE CRITERIA FOR THE DIAGNOSIS OF LEFT VENTRICULAR HYPERTROPHY*

1 Standard Limb Leads
- (a) Voltage $R_1 + S_3 = 25$ mm. or more
- (b) RS-T_1 depressed 0 5 mm or more
- (c) T_1 flat, diphasic or inverted, particularly when associated with (b) and a prominent R wave.
- (d) T_1 and T_3 diphasic or inverted in the presence of tall R waves and (b)
- (e) T_3 greater than T_1 in the presence of left axis deviation and high-voltage QRS complex in leads I and III

2 Precordial Leads
- (a) Voltage of R wave in V_5 or V_6 exceeds 26 mm
- (b) RS-T segment depressed more than 0 5 mm. in V_4 V_5 or V_6.
- (c) A flat, diphasic or inverted T wave in leads V_4 through V_6 with normal R and small S waves and (b)
- (d) Ventricular activation time in V_5 or V_6 = 0 06 sec. or more especially when associated with a tall R wave

3. Unipolar Limb Leads
- ( ) RS-T segment depressed more than 0 5 mm. in aV_L or aV_F
- (b) Flat diphasic, or inverted T wave with an R wave of 6 0 mm. or more in aV_L or aV_F and (a)
- ( ) Voltage of R wave in aV_L exceeds 11 0 mm
- (d) Upright T wave in aV_R

* From Sokolow M and Lyon, T P The ventricular complex in left ventricular hypertrophy as obtained by unipolar and precordial limb leads Amer Heart J 37 161–186 1949

record in terms of these criteria requires judgment derived from considerable experience with routine electrocardiographic interpretation Kossmann [9] discussed some of these problems in relation to one patient with left ventricular hypertrophy and rightward deviation of the mean electrical axis and another patient with right ventricular hypertrophy and left axis deviation Since ventricular hypertrophy tends to prolong the QRS interval patterns resulting from ventricular conduction disturbances are often so similar that differentiation is extremely difficult (see Fig 29)

Right Ventricular Preponderance

The electrocardiographic signs of right ventricular enlargement approximate the reciprocal of those described for left ventricular enlargement The S wave in lead I becomes very much deeper at the expense of R_I while R_{III} tends to become abnormally tall (Fig 2-) The mean electrical axis is usually shifted toward the right beyond the upper limits of normal Right ventricular hypertrophy is most commonly encountered in children in whom the vertical orientation of the heart is far more common than it is in adults For this reason, right ventricular hypertrophy in the presence of a horizontal heart is rarely encountered

Right ventricular hypertrophy with strain is illustrated in Figure -- The mean electrical axis is shifted toward the right beyond the normal range The S-T, T complexes which indicate the presence of right ventricular strain, are indicated by arrows Many other electrocardiographic patterns may be encountered among patients with right ventricular hypertrophy Myers et al [30] have discussed these patterns in detail

Explanations for the Electrocardiographic Signs of Ventricular Enlargement

The electrocardiographic signs of ventricular enlargement could be caused by various factors (a) rotation of the heart around its longitudinal axis (*vide infra*) (b) a thicker ventricular wall or (c) delayed conduction within the myocardium (e g ventricular conduction disturbances) Distinguishing between these explanations is difficult Indeed each of them has been invoked to explain the signs of ventricular hypertrophy

Kossmann et al [31] presented electrocardiographic evidence that clockwise rotation around the longitudinal axis plays an important role in the production of both the deviation of the mean electrical axis and the

LEFT VENTRICULAR HYPERTROPHY OF VERTICAL HEART

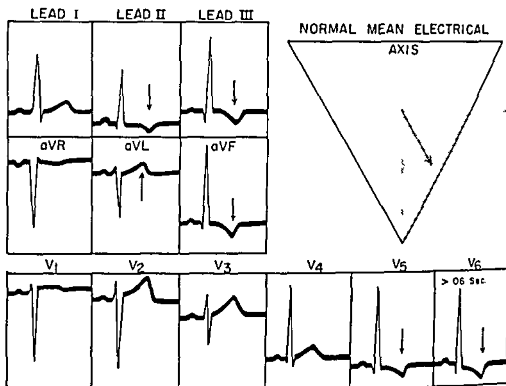


FIGURE 21 Electrocardiographic signs of vertical orientation of the heart may be counteracted by left ventricular hypertrophy in the QRS complexes of the limb leads (see Fig 15*B*) Thus the mean electrical axis may be well within the normal limits when these two conditions are coincident The principal signs of ventricular hypertrophy in this example are the inverted T waves (strain pattern) in those leads indicated by the arrows (lead II lead III aV_L aV_F and $V_{5\ 6}$) The intrinsicoid deflection in V_6 exceeds the normal limits (0 05 second) The transitional zone is at V_3 which is normal (From a record obtained through the courtesy of Dr Samuel Aronson)

left ventricular hypertrophy add weight to the diagnosis When the QRS and T waves deviate in opposite directions the typical left axis deviation of QRS is often accompanied by a deviation of the T axis to the right This phenomenon is graphically illustrated by a frontal vectorcardiogram in Figure 20 Clearly, the additional signs of ventricular hypertrophy disclosed by means of unipolar and extremity leads plus greater attention to changes in the S-T T complex have increased the incidence with which left ventricular hypertrophy is diagnosed Many patterns result from variations in the orientation and rotation of the heart The pattern resulting from left ventricular hypertrophy in a patient with vertical orientation of the heart is an excellent example of this problem

LEFT VENTRICULAR HYPERTROPHY IN A VERTICAL HEART A vertical orientation of the heart tends to produce right axis deviation, while left ventricular hypertrophy tends to shift the mean electrical axis to the left When the two conditions are combined these effects may cancel out, and the mean electrical axis may be well within the normal range Such a condition is illustrated in Figure 21 Here the QRS complexes in the standard limb leads and the mean electrical axis appear entirely normal The configuration of aV_L and aV_F indicate a vertical orientation of the heart (see Figs 14 and 15) The precordial leads reveal a transitional zone at V_3 The clues to left ventricular hypertrophy in these records are the strain patterns exhibited in a number of leads (Fig 21) The intrinsicoid deflection is greater than 0 05 in lead V_6, indicating a prolonged activation time in the left ventricle, presumably due to the thickened wall

The examples illustrated in Figures 19 and 21 obviously do not form an adequate

conduction disturbance) In 1931, Wilson MacLeod and Barker[34] pointed out the similarities between ventricular conduction disturbances and left ventricular hypertrophy They concluded that many electrocardiographic patterns attributed to hypertrophy of a ventricle are partly if not entirely due to conduction defects such as bundle branch block. Since the effects of the factors suggested by Grant and by Wilson are similar to abnormal ventricular conduction there may be little functional distinction between ventricular hypertrophy and intraventricular block Segers et al[35] presented eight cases in which electrocardiographic curves ordinarily indicative of ventricular preponderance appeared or disappeared spontaneously and were apparently caused by a peculiar intraventricular block Indeed all electrocardiographic evidence of ventricular preponderance is seriously obscured in the presence of defective ventricular conduction Although severe ventricular conduction disturbances can

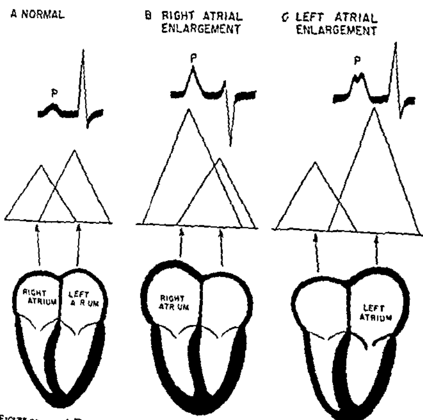


FIGURE 23 A Direct recording of electrical potentials from the surface of the atria in human patients confirms the fact that the right atrium is exci ed before the left. The P wave can be regarded as a summation of potentials from the two atria

B Right atrial dilatation produces larger right atrial potentials of longer duration leading to tall peaked P waves particularly in lead II P waves with this configuration are most frequently encountered among patients with congenital malformations of the heart (see Chapter 19)

C Broad, notched P waves occur most often among patients with mitral stenosis (see Chapter 18) but may also occur during attacks of acute rheumatic myocarditis (see Fig 10D Chapter 17) Prolongation of the P waves with notching or flattening of the summit has been related to delay in left atrial excitation and the larger potentials produced by the increased left atrial muscle mass (After Reynolds G The atrial electrogram in mitral stenosis. Brit. Heart J 15 250–258 1953)

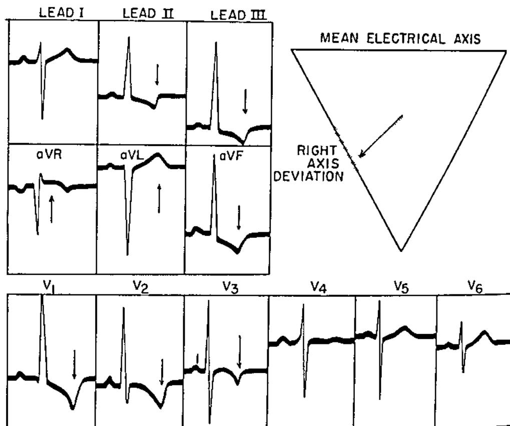


FIGURE 22 Right ventricular hypertrophy is usually indicated by a deep S_I small R_I and tall R_{III} The mean electrical axis is deviated toward the right beyond the normal range Vertical orientation of the heart is indicated by aV_R aV_L and aV_F (see also Fig 17) The transitional zone is between V_3 and V_4 Right heart strain is indicated by inversion of T waves in leads I II III aV_R aV_L aV_F and V_{1-3} This record represents a severe degree of right ventricular hypertrophy to illustrate the types of changes which may be observed Lesser degrees of right ventricular hypertrophy may present no strain patterns and less distinctive changes in the limb leads

changes in the precordial leads associated with right ventricular hypertrophy The same type of reasoning applies to left ventricular hypertrophy except that the heart rotates counterclockwise around its longitudinal axis as viewed from the apex (see Fig 15*B*)

Grant[32] has directly compared the electrical and anatomic positions of normal hearts and has found the expected relation between left axis shift and the horizontal position of the heart However, the left ventricle and interventricular septum had remarkably similar positions in the body whether the heart was normal or displayed evidence of ventricular hypertrophy In short, he found no evidence that left ventricular hypertrophy produced rotation of the heart around its longitudinal axis and concluded that detecting rotation of the heart by means of unipolar electrodes has little or no validity He explained the shift in the mean electrical axis as due to delayed transmyocardial progression of excitation through the thickened ventricular wall The potentials from the basilar portion of the left ventricle have large magnitude, being unopposed by excitation elsewhere, and the terminal QRS vectors are directed more left ward and posterior in hypertrophied ventricles than in normal hearts In 1929 Wilson and Herrmann[33] presented evidence that the average QRS interval increases with both the weight of the ventricles and the thickness of the left ventricular wall In no case did they find QRS intervals longer than 0 10 second, so they concluded that greater prolongation of the QRS interval must be due to some other factor (e g , ventricular

the two electrodes the QRS complexes are apt to be slurred notched or multiphasic (e g in lead III from patients with hearts oriented in the horizontal position as in Fig 18) On the other hand the development of slurring or notching of the QRS complex during cardiac disease (e g, acute myocarditis) may have diagnostic significance when correlated with other clinical and electrocardiographic evidence (see Chapter 17) Slurred or notched QRS complexes develop during a disease process when the rate or sequence of ventricular excitation changes locally Delayed conduction over small portions of the ventricular walls may distort QRS complexes in a single precordial lead a condition which has been called focal block 37 38

Intraventricular Block

Grossly prolonged and distorted QRS complexes are generally attributed to a block in the main branches of the bundle of His (right and left bundle branches) Interference with conduction along the right bundle branch would delay the arrival of excitation in the right ventricular wall (Fig 25A) In this case the following sequence is postulated (a) atrial excitation beginning at the sino-atrial node follows a normal course so the P wave and P R interval are essentially normal (b) excitation of the left side of the septum and the left ventricular wall proceeds at normal speed (c) the right ventricular wall is invaded after considerable delay by a wave of excitation along the slowly conducting myocardial fibers or by way of Purkinje bundles excited below the region of the block Although the proximal portions of the bundle branches are generally indicated as the site of blocked conduction a widespread interference with conduction in the peripheral distribution of the Purkinje fibers (e g at the junction of the Purkinje fibers with the myocardium) could have similar functional and electrocardiographic effects The initial deflections of the QRS complexes are sharp and brief while the subsequent deflections are delayed slurred and deformed When the right ventricular wall is depolarized late the mean electrical axis tends to be directed from the center of the chamber toward the right ventricle (right axis deviation) The prolonged and slurred deflections are directed downward in lead I and upward in lead III Repolarization begins in the regions activated first and tends to follow the same general course as the depolarization. Thus the T wave is deflected in a direction opposite from that of the most prolonged QRS wave The segment between the QRS and T waves is usually displaced

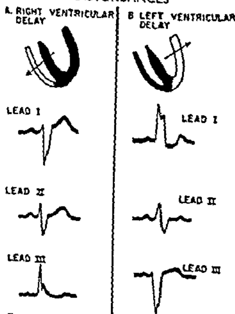


FIGURE 25 *A* A ventricular conduction disturbance which delays the arrival of the wave of excitation to the right ventricle produces prolongation of the ventricular depolarization and wide QRS complexes an example of which is shown. The mean electrical axis is deviated to the right, beyond the normal limits in this case (arrow) The T waves tend to deflect in a direction opposite to the direction of the mean QRS deflection. This type of conduction disturbance is generally called right bundle branch block.

B Delayed conduction to the left ventricular myocardium produces abnormal electrocardiographic patterns in the standard limb leads with the deformed portion of QRS predominantly upward in lead I and downward in lead III The mean electrical axis tends to deviate to the left. However the mean electrical axis is usually not equivalent to the resultant of the instantaneous electrical axis when severe conduction disturbances are present (see Fig 26)

occur when there is no other evidence of cardiac disease (Fig 26), they are usually associated with ventricular hypertrophy Thus, deviations of the mean electrical axis beyond the expected range should stimulate a search for other signs of ventricular hypertrophy, regardless of the cause of the axis shift

Although ventricular preponderance is one of the most common electrocardiographic interpretations, the criteria used by various authorities are remarkably diverse Dimond[36] quoted the answers given by eight authorities in response to the simple question "What are the electrocardiographic evidences of left ventricular hypertrophy " No two answers were alike, and the divergence of opinion was extreme Of five authorities asked the normal limits of the intrinsicoid deflection, three stated they did not use this measurement It is very important to recognize that interpreting configurational changes in deflections remains a highly subjective process which depends in large measure on the experience and attitudes of the individual

Right Atrial Dilatation

Enlargement of the right atrium tends to increase the total mass of atrial musculature, and a larger solid angle is subtended during depolarization (Fig 23) Tall peaked P waves particularly in lead II frequently occur in conditions which produce right atrial dilatation The P wave pattern illustrated in Figure 23*B* is commonly called P pulmonale because it is often associated with pulmonary hypertension from primary disease of the lungs Similar changes are also encountered in many congenital malformations of the heart (Chapter 19)

Left Atrial Dilatation

Distention of the left atrium prolongs its depolarization, and the P waves become broad, flattened and notched, particularly in leads I and II (Fig 23C) This P wave pattern occurs with rheumatic mitral valvular stenosis and has been called P mitrale (see Chapter 18)

ELECTROCARDIOGRAPHIC SIGNS OF ABNORMAL VENTRICULAR CONDUCTION

Whenever a portion of the specialized conduction system in the ventricles is non functional, the excitatory process must traverse the slowly conducting myocardial fibers Thus, excitation is delayed in the myocardium served by the affected portion of the conduction system If excitation of a sufficient mass of myocardium is delayed, the QRS interval is prolonged and the configuration of the QRS complexes is altered (see also Fig 13, Chapter 14)

Slurring and Notching of the QRS Complex

Slurring or notching of the QRS deflections in standard limb leads is frequently ignored in electrocardiographic interpretation because either may occur in normal individuals (Fig 24) Whenever the wave of excitation travels in a direction approximately perpendicular to a line connecting

SLURRING AND NOTCHING OF QRS COMPLEX

A SLURRING



B NOTCHING

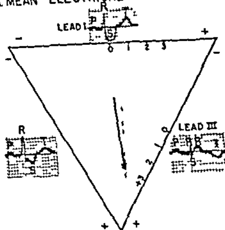


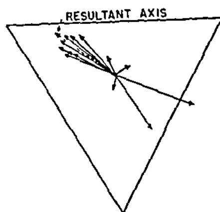
FIGURE 24 Minor variations in the configuration of the QRS complex are frequently observed in electrocardiograms from individuals with no evidence of heart disease

A Slurring of the QRS complex indicates that the spread of excitation is moving in one direction longer than usual this may either be fortuitous or indicate delayed depolarization in some area

B Notching of QRS complexes represents a slightly more advanced degree of conduction delay These changes have no diagnostic significance unless they develop during the course of a febrile illness (e g myocarditis Chapter 17)

MEAN ELECTRICAL AXIS IN VENTRICULAR CONDUCTION DISTURBANCES





C VECTORCARDIOGRAM



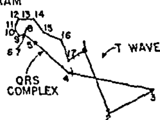


FIGURE 26 Electrocard ographic records from a 24 year-old medical student with no history or evidence of cardiac disorder revealed a severe ventricular conduction disturbance The P R interval was 0 20 and the QRS interval was 0 16 second.

A A mean electrical axis determined in the routine fashion was +85 degrees

B Instantaneous electrical axes computed for each 0 01 second during the QRS complex were directed primarily upward and toward the right shoulder so the resultant axis was approximately −140 degrees The reason for the d screpancy between the mean electrical axis and the resultant of the instantaneous axes was the fact that the amplitude of the deflections failed to indicate the time during which the potentials were present particularly when certain portions of the QRS were slurred and grossly prolonged

C Frontal vectorcardiograms drawn from the instantaneous vectors and directly recorded from a cathode ray oscilloscope are presented for comparison (From Merrill C. F Minor R H Paton R R and Shields J R An analysis of some aspects of vectorcardiography Student Project Reports Department of Physiology and Biophysics University of Washington)

a resultant vector can be derived which is called the ventricular gradient Changes in the ventricular gradient result from variations in the duration of the excited state in the myocardium as it is affected by changes in its functional condition When a method is developed by which the ventricular gradient can be routinely determined it will be possible to differentiate more readily between the alterations in the S-T T complex due to changes in the *sequence* of repolarization (ventricular conduction disturbances) and those due to changes in the *rate* of repolarization [40 41]

Premature Ventricular Contractions

Ventricular excitation follows an abnormal course and sequence when a premature con

from the baseline There is no period when the ventricles are completely depolarized, and there is no isoelectric S-T segment

Conversely, in left bundle branch block, conduction to the left ventricular wall may be delayed while the endocardial surface of the right ventricular cavity is excited promptly (Fig 25*B*) Under these conditions, waves of excitation spread more or less simultaneously through the free wall of the right ventricle and through the interventricular septum By the time a wave of excitation reaches the left ventricular wall, depolarization of the right ventricle and the septum is largely complete Thus, the final deflection of the QRS is prolonged, slurred and deformed because it results from retarded activation of the left ventricular wall, unopposed by activity in the remainder of the heart (Fig 25*B*) The prolonged QRS wave is generally downward in lead III and upward in lead I, and the T waves deflect in the opposite direction

Clearly, alterations in the rate and sequence of excitation and repolarization can produce an unlimited variety of wave forms on the electrocardiographic records All degrees of intraventricular conduction disturbance from simple slurring and notching of QRS deflections to grossly deformed and prolonged QRS complexes are encountered during routine electrocardiographic interpretation Since the correlation between pathologic lesions in the vicinity of the bundle branches and the electrocardiographic signs has been controversial, the rather complicated classification of such conduction disturbances has questionable value For these reasons it may be preferable to lump all the ventricular conduction disturbances into the single classification, intraventricular block [39] A notation of right or left ventricular delay may be warranted when electrocardiographic signs are clear (Fig 25)

The Mean Electrical Axis with Abnormal Ventricular Conduction

When the waves of excitation pursue abnormal courses through ventricular myocardium, the instantaneous and mean electrical axes generally deviate from their normal orientations The mean electrical axis, determined in the routine manner (Fig 15), approximates the resultant of the instantaneous vectors only *so long as the height of the individual deflections is proportional to the area under them* If each deflection of the QRS complexes conformed to an isosceles triangle subtending the same apical angle, the height of the deflection would be proportional to its duration and would therefore be proportional to the area under the deflection When a deflection is markedly prolonged, its height is not related to the duration of the deflections and the mean electrical axis and the instantaneous vectors usually point in entirely different directions A rather extreme example of discrepancy between the mean electrical axis and the instantaneous vectors is illustrated in Figure 26 Instantaneous electrical axes were computed at intervals of 0 01 second for comparison with frontal vectorcardiograms The mean electrical axis was also computed and was found to subtend an angle of about +85 degrees In contrast, most of the instantaneous axes were directed in quite another direction, so their resultant vector was directed at about −140 degrees Mistakes of this type could be avoided by using the area under each deflection in the QRS complex to compute the mean electrical axis This can be accomplished by counting the small squares and fractions thereof which lie inside the area bounded by the deflection and the baseline Each square represents 4 microvolt seconds (sometimes called an Ashman unit) The mean area axis of the QRS can then be computed by determining the net positive and negative QRS areas of leads I and III and entering them on an Einthoven triangle If this time-consuming procedure is used, the mean area-axis of QRS (designated ÂQRS) should conform closely to the resultant of the instantaneous vectors in the example illustrated in Figure 26 From ÂQRS and the mean area-axis of the T wave

the S-T segment and T wave changes in the T wave are often but not always associated with the duration of the S-T segment It is not considered appropriate to embark upon a comprehensive discussion of the many factors which can affect repolarization Certain causes of altered S-T T complexes are mentioned because they pertain to subjects covered in the subsequent chapters

Abnormal Sequence of Repolarization

As indicated in the preceding section ventricular conduction disturbances delay excitation of certain regions of the heart walls and correspondingly retard completion of repolarization in those areas The abnormal sequence of excitation is reflected in an abnormal sequence of repolarization which changes the configuration of the S-T T complex Generally the S-T T complex and the main (prolonged) QRS deflection deviate in opposite direction (see Figs -5 27) This signifies that in abnormal cycles the process of repolarization follows the sequence of excitation more nearly than it does in normal cycles Thus the changes in S-T T complex coincident with an abnormal course of ventricular excitation result from an abnormal sequence of repolarization

Abnormal Degrees of Polarization

Changes in the functional state of the myocardial fibers can change the extent of polarization For example whenever the S-T segment and the T-Q segment are isoelectric the ventricular myocardium is uniformly depolarized during systole and uniformly polarized during diastole (Fig 28A) If during diastole the depolarized state persisted in a region of myocardium sufficiently large to affect external electrodes a potential difference would exist which would depress the T-Q interval below the S-T segment (Fig 28B) If the same region remained partially polarized during both systole and diastole precisely the same electrocardiographic pattern would be produced with the S-T segment elevated and the T-Q segment depressed (Fig 28C) Finally if the same area remained polarized throughout the cycle a potential difference

ABNORMALITIES IN THE EXTENT OF POLARIZATION AND REPOLARIZATION

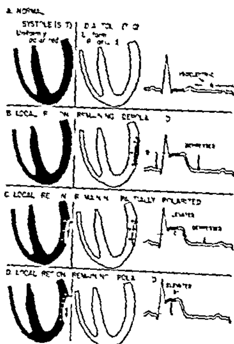


FIGURE 28 A When the ventricular myocardium is uniformly polarized or depolarized no potentials can be recorded by an external electrode (see Fig 6B) For this reason, the S-T and T-Q intervals are normally isoelectric

B If a local region in the left ventricle remained depolarized during diastole a potential difference would exist between the polarized and depolarized regions The junction between these two zones could be represented by a charged membrane with the negative charges facing the exploring electrode as indicated above At this electrode a negative potential would produce a downward deflection during diastole (T-Q interval) but not during systole Thus the T-Q segment would be displaced downward in relation to the S-T segment. If the local region became partially polarized the T-Q segment would be displaced but not quite so far

C If a region remained partially polarized to the same extent during both systole and diastole the S-T segment would be somewhat elevated and the T-Q interval would be similarly depressed producing a picture very similar to that indicated in *B* above

D If a local region remained polarized through the cycle the S-T segment would be elevated in relation to the T-Q segment If the exploring electrode were placed on the opposite side of the heart the S-T and T-Q segments would be displaced in the opposite direction. (Adapted from Kossmann.[4])

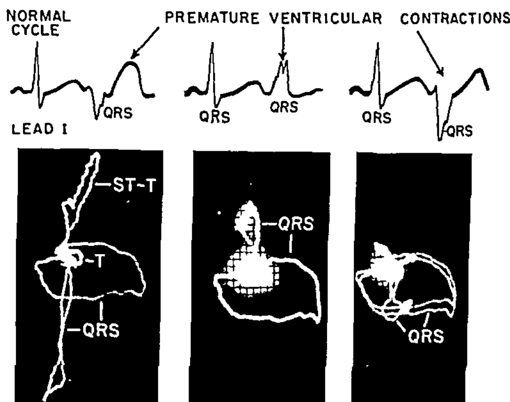


FIGURE 27 An electrocardiogram is presented in which every normal cycle was followed by a premature ventricular contraction (coupling) However at least three irritable foci in the ventricles were discharging impulses at one time or another Changes in electrocardiographic and frontal vectorcardiographic patterns produced by the abnormal ventricular conduction from three ectopic foci are illustrated

traction is initiated at some ectopic focus in the ventricular myocardium (see also Chapter 14) Distorted QRS complexes of widely varying form are produced by this mechanism Premature ventricular contractions generally begin without a P wave very shortly after the T wave of a preceding normal cycle The QRS-T pattern varies with the origin and course of the wave of excitation The configurations of complexes initiated by different ectopic foci are illustrated in Figure 27

The patterns inscribed during normal cycles were very reproducible while the premature ventricular contractions varied widely The general direction taken by the wave of excitation as projected on the frontal plane is indicated by the QRS loops on the vectorcardiogram Considerable discrepancy between the mean electrical axis and the resultant of the instantaneous vectors occurs with premature ventricular contractions just as with ventricular conduction disturbances (Fig 26)

ABNORMALITIES OF VENTRICULAR REPOLARIZATION (S-T, T)

In contrast to the process of excitation which is rapidly distributed by a specialized conduction system the sequence of repolarization depends only on the duration of the depolarized state in the various myocardial fibers The duration of the excited state is varied by temperature pressure, electrolyte concentration (e g potassium, calcium) and other factors such as administration of various drugs and the oxygen supply, as they affect the physiologic condition of the myocardium For this reason the T wave has the most labile configuration of all the major deflections Since the repolarization process occurs during the inscription of both

ELECTROCARDIOGRAPHIC CHANGES IN VARIOUS CONDITIONS

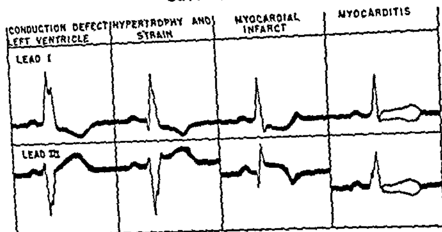


Figure 29 In both ventricular conduction disturbances and ventricular hypertrophy with strain the QRS complex tends to be prolonged and the S-T T complexes are generally displaced in a direction opposite the main QRS deflection. A similar pattern may be produced by a myocardial infarction on the posterior aspect of the heart except for the presence of Q_{III} and deviation of S-T and T in opposite directions. Changes in QRS S-T and T waves of almost any type can be produced in the course of acute inflammatory disease of the myocardium (myocarditis) Because of their basic points of similarity distinguishing these different conditions by their electrocardiographic patterns is often very difficult.

point, electrocardiographic patterns which might be encountered in each of four very different disease states are presented in Figure 29 Although certain characteristic differences can be described to distinguish the patterns produced by ventricular conduction disturbances ventricular hypertrophy and strain myocardial infarction and myocarditis the basic similarities in the patterns must not be overlooked In less extreme examples the differences may be difficult to distinguish particularly when more than one of these conditions is present in one patient While a truly remarkable amount of important information can be gleaned from a routine electrocardiographic examination by a competent cardiologist his interpretation must always be viewed in relation to all other sources of information concerning the patient under consideration By correlating the electrocardiographic patterns with other signs and symptoms a large number of disease states can be excluded from the differential diagnosis and a specific diagnosis often can be made Serial electrocardiograms taken at appropriate intervals and accompanied by parallel clinical studies during the progress of a disease state will frequently establish a diagnosis when the cardiac status is in doubt at the initial examination

Since electrocardiographic interpretation has been approached on a theoretical basis the empirical approach has been neglected This aspect of the subject will be further considered in relation to specific disease states (see Chapters 16 17 18, 19) However for a comprehensive discussion of electrocardiographic interpretation the reader is referred to standard texts on the subject

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during electrical systole would elevate the S-T segment (Fig 28D) Whenever a region of myocardium retains the same degree of polarization through a cardiac cycle, identical patterns can be produced by any one of the three mechanisms illustrated in Figure 28 The only difference between the three patterns lies in the level of a "zero" potential, which cannot be distinguished on electrocardiographic records This approach to understanding the electrocardiographic effects of myocardial injury was discussed in detail by Kossmann[42] The mechanism illustrated in Figure 28B has been utilized to explain the deviation of the S-T segment which occurs during myocardial infarction This subject will be considered further in Chapter 16

Abnormal Rates of Repolarization

Although the myocardium might ultimately reach uniform polarization and depolarization, acceleration or retardation of these processes can affect the levels of the S-T and T-Q segments For example, if a region of the myocardium remained depolarized for an abnormally long time, potential differences similar to those illustrated in Figure 28B would become manifest during the latter part of the S-T segment The S-T segment would ascend and terminate in a tall T wave This mechanism actually operates in causing the abnormal S-T and T complex associated with severe ventricular conduction disturbances in which delayed depolarization produces delayed repolarization In contrast therapeutic doses of digitalis accelerate the process of repolarization If the rate of repolarization is not uniform throughout the ventricular myocardium, the S-T segment is displaced and the T wave is altered Changes in the concentration of certain electrolytes in and about the myocardial cells also affect the repolarization process For example, if the concentration of calcium in the blood is abnormally low, the process of repolarization is prolonged, which is evidenced by prolongation of electrical systole (Q-T interval) High blood calcium levels have the opposite effect Hypopotassemia also changes the duration of the Q-T interval and alters the S-T, T complex Goldberger[26] proposed that the ventricular strain pattern (Fig 29) is related to a loss of potassium from the myocardial fibers of a ventricle under stress Inflammatory processes in the myocardium may produce widely diversified changes in all the electrocardiographic complexes including the S-T, T complex (see Chapter 17)

Direct information concerning the rate and sequence of repolarization is scarce Not even the rate and sequence of repolarization of normal ventricles have been described to say nothing of the changes which result from disease For this reason, the interpretation of the configurational changes in the S-T complex is almost completely empirical

SUMMARY

The fundamental difficulty in electrocardiographic interpretation stems from the fact that the changes in configuration of the complexes are rather nonspecific and limited in number For example, the QRS and T waves can have major deflections upright, downward or deformed The S-T segment can be isoelectric, elevated, depressed or curved Since a vast number of disease states may directly or indirectly affect the electrocardiographic complexes certain electrocardiographic patterns must be common to many different pathologic conditions The theoretical approach which has been followed in this chapter emphasizes the fact that interpreting changes in the configuration of individual waves and complexes frequently involves recognizing rather subtle differences which have been discovered empirically Contrary to the usual discussion of electrocardiography, the points of similarity between complexes and mechanisms have been emphasized rather than the differences which can be demonstrated by selected examples This attitude is not intended to depreciate or cast doubt upon electrocardiographic interpretation but to help place it in a proper perspective To illustrate this

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Part Five

DIAGNOSIS OF CARDIAC DISEASE

Myocardial Ischemia

All too frequently, myocardial ischemia is considered solely as a manifestation of coronary arterial disease. Actually, the coronary flow must be viewed in relation to the myocardial oxygen requirements and the total energy release of the heart. The coronary blood flow is only one factor which may limit the cardiac reserve (see Chapter 8). Myocardial ischemia results from relative coronary insufficiency during both normal and abnormal conditions primarily from increased oxygen consumption by the myocardium rather than from the curtailing of coronary blood flow. This occurs in normal persons during strenuous exertion. When the myocardium is supplied with an adequate blood flow, it can accomplish prodigious amounts of work. A critical *stage in* heart disease is most often reached when oxygen delivery is insufficient for the oxygen consumption during normal activity. Even in advanced stages of cardiac disability the cardiac output and oxygen delivery may be entirely adequate at rest. However, under such circumstances the cardiac reserve capacity diminishes to the point that it reduces the *maximum* activity the individual can sustain. The status of a patient should be evaluated in terms of the relationship between the load on the heart and the factors which might interfere with *the transportation* of oxygen into the myocardial cells.

GENERAL CAUSES OF MYOCARDIAL ISCHEMIA

Many types of cardiovascular disease impose an increased load on the heart and at the same time interfere with oxygen delivery to the myocardium (see Chapter 8). A few additional examples are cited.

Pressure Loads

Arterial hypertension increases the work of the heart and leads to hypertrophy of the muscle fibers which in turn increases the diffusion distance between the coronary capillaries and the center of the myocardial cells (see Fig. 6, Chapter 8). Since arterial hypertension is usually associated with some degree of arteriosclerosis, blood flow through the coronary arteries may be impeded. Whenever a load on the heart is compensated *by an increase in the myocardial* mass in the cardiac walls, the *efficiency of* oxygen delivery to the heart is diminished to some *extent*.

Similarly, aortic valvular stenosis imposes a serious pressure load on the left ventricle and simultaneously diminishes the pressure gradient from the root of the aorta to the coronary capillaries (see Chapter 17). Blood flow through the coronary arteries may cease completely during ventricular systole.

Volume Loads

Abnormally great ventricular output results *from a number of* conditions. In any form of valvular insufficiency, stroke output increases to compensate for the volume of blood which regurgitates (see Chapter 17). Aortic regurgitation produces a pernicious volume load on the left ventricle because the low *diastolic* pressure in the root of the aorta reduces the pressure driving blood through the coronary arteries. A similar functional disturbance results from arteriovenous *shunts* or from patent ductus arteriosus (see Chapter 19).

Diminished Oxygen Transport

Primary pulmonary disease may interfere

Introduction to Part Five

To illustrate the applications of physiologic principles to specific problems of diagnosis five broad categories of cardiac disease have been selected for consideration Abnormal cardiac function as a direct result of changes in the heart walls is produced by deficient blood supply to the myocardium (*Myocardial Ischemia*, Chapter 16) or by inflammatory processes (*Myocarditis* Chapter 17) The former is primarily a disease of the aged and the latter most commonly occurs in children and young adults Inflammatory diseases of the heart and arterial trunks may produce deformity and malfunction of the cardiac valves which impose sustained volume or pressure loads on the heart (*Valvular Disease*, Chapter 18) Developmental defects in the valves and partitions of the heart also produce pressure and volume loads which generally become manifest shortly after birth (*Congenital Heart Disease*, Chapter 19) When the patterns of diagnostic signs and symptoms are incomplete a diagnosis of *possible* heart disease may be warranted (Chapter 20) This term is most appropriately applied to patients exhibiting only one abnormal sign or symptom

Although this selection of cardiac abnormalities is not inclusive a majority of patients with heart disease fit into one or more of these categories Discussions of these various disease entities include both a description of the distinguishing features of each and the similar features which may be encountered in widely different disease processes

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Diminished Oxygen Transport

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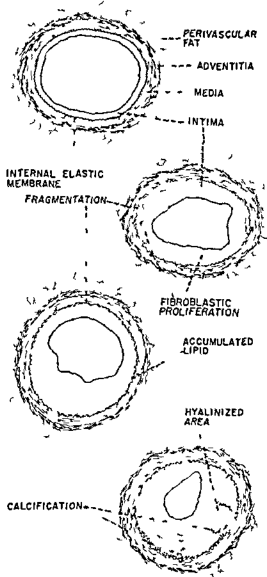


FIGURE 1 In the normal coronary artery the intima is uniformly thin and composed of collagenous connective tissue The early stages of coronary atherosclerosis are characterized by fragmentation of the internal elastic membrane and thickening of the intima due to fibroblastic proliferation associated with accumulation of mucopolysaccharide Mucopoly saccharides are long-chain molecules contributing to the gelatinous state of interstitial fluids (see Figs 6 and 7 Chapter 9) In the early phases of the process accumulation of lipid may or may not be demon strable[2] As the *intima becomes thickened lipids* (e g cholesterol) tend to accumulate at the junction of the intima with the media Finally areas of the atherosclerotic plaque degenerate and become hyalinized *Calcium is deposited predominantly at the* edges of hyaline areas and at the junction of intima and media The lumen of the vessel is greatly restricted and may even become completely occluded by progressive expansion of the atheroma

with oxygenation of the blood in the lungs, so that arterial blood contains reduced quantities of oxygen to supply both the tissues and the myocardium At the same time, pulmonary arterial hypertension may impose a pressure load on the right ventricle

Clearly, the principles indicated by these few examples could be extended to encompass most forms of *cardiovascular disease* Thus, myocardial hypoxia is an important factor to be considered in evaluating any *patient with cardiovascular disease* This chapter is devoted primarily to myocardial ischemia produced by functional and or*ganic disturbances in the coronary vessels* with a brief summary of the effects of various metabolic diseases

CORONARY ATHEROSCLEROSIS

The principal cause of restricted coronary flow results directly or indirectly from atherosclerosis Although its cause has not yet been determined, atherosclerosis is no longer considered a degenerative process to be expected with advancing age It is now regarded as a metabolic disturbance of lipid metabolism, for which specific therapy may be ultimately developed[1] This change in attitude is a most important development for future progress

The Nature of Coronary Atheromata

Atherosclerosis occurs with greatest frequency *in the aorta and in the cerebral* and coronary arteries In Figure 1, the pathogenesis of atherosclerotic lesions in the *coronary arteries is illustrated* schematically in accordance with the sequence of events described by Moon and Rinehart[2] Early *lesions are characterized by diffuse* thicken ing of the intima due to accumulated mucoid ground substance and proliferation of subendothelial fibroblasts The internal elastic membrane is fragmented by focal areas of degeneration Accumulation of lipids is not always demonstrable in early lesions, and its

localization in intima media or in both is somewhat unpredictable

When coronary atherosclerosis is well developed the intima is thickened by fibrous proliferation the advancing borders of the plaques being composed of loosely arranged fibroblasts and mucoid ground substance (mucopolysaccharide) resembling the early lesions Lipid accumulates as fine and coarse droplets principally at the base or center of the plaque and least along the endothelial border The intimal plaques often encroach upon the media

Advanced stages of atherosclerosis are characterized by hyaline degeneration at the base or center of the plaques where the concentration of lipid is greatest Calcification usually begins at the junction of the intima and media or in the hyalinized areas The elastic tissue suffers extreme degeneration and fragmentation Infiltration of the adventitia with lymphocytes is frequently observed. The histologic appearance of atherosclerotic lesions is illustrated by the photomicrographs in Figure 2

The Incidence of Coronary Atherosclerosis

The initial stages of coronary atherosclerosis are observed in virtually all adults If rigid criteria are used only very young children are completely free of any stigmata The incidence and severity of atherosclerotic lesions in the coronary arteries increases with age White, Edwards and Dry[3] tabulated the degree of coronary atherosclerosis observed during 100 consecutive autopsies on men whose ages were distributed through the six decades between 30 and 89 years Some results of this study are summarized in Figure 3 The average severity of the lesions increased very rapidly from age 30 through 49 years The lesions in the right main coronary artery and in the two main branches of the left coronary artery (anterior descending and circumflex) were comparable On the average the plaques were less extensive in the smaller branches of the right coronary artery (posterior descending and right marginal) This study indicates that the severity of atherosclerotic lesions tends to

HISTOLOGY OF CORONARY ATHEROSCLEROSIS

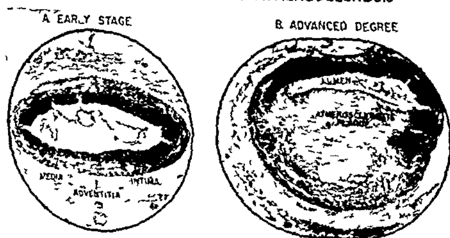


FIGURE 2 Two photomicrographs of a main coronary artery (on the right) and a small branch of the same vessel (on the left) illustrate the histologic appearance of early and advanced coronary atherosclerosis

A The intima is irregularly thickened to a very slight degree. Slight fragmentation of the internal elastic media is present, but not effectively reproduced in this photomicrograph. In other respects the vessel is normal.

B The lumen of this large coronary artery is greatly reduced by a large atherosclerotic plaque. Fusiform vacuoles in the intima remain where lipids were dissolved away The intima is grossly thickened by processes illustrated in Figure 1 A hyalinized area appears in the basilar portion of the plaque Lymphocytes have infiltrated a region around the periphery of the adventitia at the bottom of the photomicrograph.

DEVELOPMENT AND DISTRIBUTION OF CORONARY ATHEROSCLEROSIS

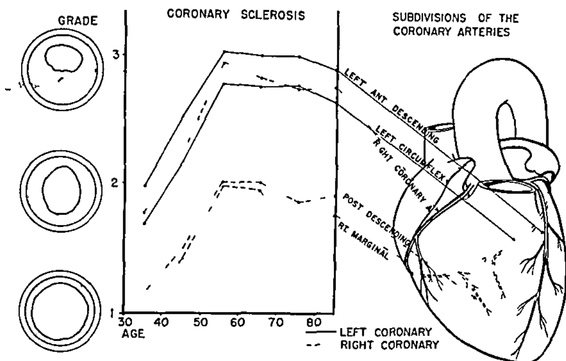


FIGURE 3 The most severe atherosclerotic lesions in each subdivision of the coronary arteries were determined in 100 consecutive postmortem examinations on men in each decade from 30 through 89 years The average grade of the most severe lesion was plotted for each decade of life in each segment of the arterial tree Similar degrees of atherosclerotic changes were noted in the right main coronary artery and in the anterior descending and circumflex branches of the left coronary artery Smaller branches of the right coronary artery had less severe lesions (After White Edwards and Dry [3])

remain fairly constant after the fifth decade About 70 per cent of the men who had passed their fifth decade had sclerosis of grade 3 or more somewhere in the distribution of the coronary arterial system

Functional Effects of Coronary Obstruction

Expanding atheromatous plaques seriously restrict the lumen of the coronary arteries (Figs 1, 2) The diminished lumen increases the resistance to the flow of blood past the site of atherosclerotic lesions Thus the pressure drop along the vessel is greater than normal and the perfusion pressure in the distal branches is diminished Since the pressure gradient is very shallow in large arteries, their lumen can be considerably diminished without a significant reduction in the pressure head beyond the obstruction In small arteries, the same reduction in the lumen produces a much greater pressure drop Coronary atherosclerosis is usually not an isolated lesion, but a number of lesions scattered throughout the coronary arterial tree Some of the arterial pressure head is lost as the blood passes each obstruction (Fig 4) Vasodilatation of the small coronary vessels[4] helps compensate for increased resistance upstream However, the compensatory dilatation of the coronary bed is limited so that encroachment on the lumen of an artery beyond some critical degree will produce progressive diminution in blood flow

Atherosclerosis develops gradually and may completely occlude a large branch of a coronary artery without causing destruction of the myocardium because collateral channels from adjacent branches expand and carry additional blood to maintain the viability and function of the affected area [5, 6] Widespread coronary atherosclerosis is occasionally observed in postmortem examina

tion of patients who had no previous disability attributable to insufficient blood flow to the heart. Experimental coronary occlusion has clearly indicated the importance of the rate at which obstruction develops.

EXPERIMENTAL CORONARY OBSTRUCTION. If a major branch of the coronary arteries in a dog is gradually occluded over a period of weeks or months neither histologic evidence of myocardial damage nor reduced ventricular performance may be demonstrable.[7] Progressive occlusion of two main coronary branches may also be well tolerated. Dogs which survived this procedure ran at 3 m p h on a grade of 25 degrees for 30 minutes without difficulty. One animal survived successive ligation of all three major branches of the coronary arteries. The septal and conus arteries must have been the principal remaining source of blood to the ventricles. A similar degree of coronary obstruction has been described in humans.[8, 9] In about half of human hearts an artery arises from a separate ostium near the right coronary artery to supply the pulmonary conus.[8, 9] This artery may provide substantial collateral flow when the other vessels are more seriously afflicted with atherosclerosis.

Even moderate degrees of atherosclerosis presumably limit the cardiac reserve. Since coronary venous blood contains very little oxygen a reduction in the arteriovenous oxygen difference would do little to remedy the deficiency (see Chapter 8). Complete occlusion of one or more major branches of the coronary arteries must diminish the *total* coronary reserve even though collateral channels dilate to serve myocardium deprived of its blood supply. Since atherosclerotic plaques are usually not restricted to one or two coronary branches (Fig 3) collateral channels generally connect vascular networks with varying degrees of sclerosis.[10] Considering the fact that atheromata usually appear in several coronary trunks the degree of coronary sclerosis which can develop without seriously limiting the exercise tolerance is almost unbelievable.[8, 10] The disparity between the extensive pathologic involvement of the coronary arteries and the limited degree of functional disability is difficult to explain. However such discrepancies between organic disease of the heart and its powers of compensation are not only commonplace, but a constant source of difficulty in predicting the course of cardiovascular disease. This fact indicates that undetected factors play a role in these compensatory reactions.

HYDRAULIC EFFECTS OF VASCULAR OBSTRUCTION

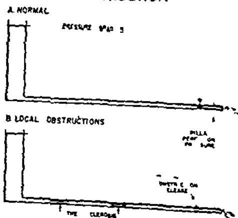


FIGURE 4. *A*, Fluid is propelled rapidly through vessels of large caliber by shallow pressure *gradients*. *Pressure* declines steeply wherever the caliber is greatly diminished. In the coronary vessels the pressure gradient steepens as the vessels ramify to smaller and smaller caliber but the greatest pressure drop occurs at the terminal vessels where peripheral resistance is controlled.
B, Atherosclerosis produces local obstructions consisting of segments in which the lumen is greatly restricted as indicated schematically in the drawing. Steep pressure gradients at each restricted segment of vessel may *dissipate much of* the total pressure head before the blood reaches the terminal branches. Peripheral vasodilatation compensates for the increased resistance upstream but *the* reserve coronary flow is depleted in the process.

ANGINA PECTORIS

The most common symptom of impaired coronary flow is precordial pain. Patients with coronary atherosclerosis may develop a syndrome consisting of a fairly specific constricting type of pain which seems to originate behind the sternum and frequently radiates over the left precordium and along

the inner surface of the left arm The term "angina pectoris" is applied to this particular type of pain, which characteristically occurs in paroxysms of relatively brief duration, brought on most commonly by exertion or any other activity which increases the cardiac output Walking rapidly uphill against a cold wind is perhaps the most frequently cited set of circumstances precipitating an attack The discomfort is often accompanied by a sensation of impending doom, causing the patient to stop in his tracks until the pain recedes

Etiology of Angina Pectoris

Myocardial ischemia is the logical precipitating cause of angina pectoris Anginal pain is usually compared to the pain produced by exercising the muscles of the forearm when their blood supply is cut off by an inflated cuff Acid metabolites tend to accumulate in muscles contracting without an adequate oxygen delivery, and these substances may stimulate pain endings directly or through changes in *p*H

Inadequate blood flow through the coronary arteries is the principal underlying feature of the disease and may result from (*a*) increased resistance to coronary flow, (*b*) reduced perfusion pressure, (*c*) increased oxygen requirements of the myocardium or (*d*) a combination of these factors Increased resistance to coronary blood flow stems from coronary atherosclerosis, coronary spasm or both Coronary spasm is generally assigned an important role in angina pectoris because of its brief duration, and because of the facts that strong emotions may precipitate an attack, the pain disappears with rest, and clinical signs may be absent between attacks The relief of pain after administration of nitroglycerin also indicates that coronary spasm existed during attack

In general, angina pectoris can be produced by any set of conditions which simultaneously impose a load on the heart and impede coronary blood flow However the picture is not as clear as this statement implies because many patients have severe angina, apparently without sufficient changes in coronary vessels, and others have no angina even after attacks of acute coronary occlusion Furthermore, not all patients have the typical retrosternal pain with radiation to the left arm The pain may be referred to different regions over the precordium or back and to more distant sites These deviations from the typical response must be related to the perception and radiation of pain from the heart

Characteristics of Visceral Pain from the Heart

The pain of angina pectoris is described variously as a constriction, a burning sensation, a fullness or tightness in the chest, a choking sensation, or an uncomfortable aching discomfort Most commonly, the pain seems to be centered just behind the mid-portion of the sternum, radiating predominantly to the left precordium, but occasionally extending to the epigastrium, the root of the neck, the jaw, the shoulder, the back, and down the arms (usually the left) In contrast with somatic sensations of touch or pain evoked from the skin, visceral sensation is characteristically poorly localized Somatic pain in many regions of the body is recognized as coming from a very discrete area, this can be easily demonstrated by pricking the finger or tongue with a pin Nerve endings are very close together in these regions, and are stimulated with sufficient frequency that localization is learned at an early age On the skin of the back the point of stimulation cannot be as accurately recognized, apparently because the sensory nerve endings are farther apart Nevertheless the site of the stimulus is perceived as being within a circumscribed area on the skin Conversely pain produced by a needle thrust through the skin into skeletal muscles or into a blood vessel may produce a diffuse, deep aching sensation which involves a large area, even an entire arm or leg Inaccurate localization and diffuse distribution of pain from viscera are the basis for the radiation of pain in angina pectoris

Radiation of Anginal Pain

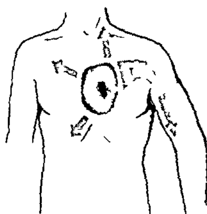
The frequent radiation of cardiac pain from the precordium to other regions (Fig 5 A) indicates that visceral afferent fibers must have central connections in common with the somatic afferent system

In 1893 MacKenzie[11] suggested that sensory impulses from the viscera have no direct connection with the brain, but act as an irritable focus in the segment at which they enter the spinal cord He postulated that afferent impulses from viscera reinforce or facilitate impulses from the somatic afferent nerves producing perceptible pain On the other hand Ruch[12] has suggested that visceral afferent and somatic afferent fibers may converge on the same neurons in the spinal cord or at higher levels so that painful sensations from a viscus are perceived on the basis of experience as coming from the distribution of the somatic nerve If convergence can exist between the somatic and visceral afferent systems it is not surprising that pain from the heart is referred to distant regions served by the somatic efferent nerves According to Wyburn-Mason,[13] cardiac pain is usually referred to the left side of the body because nerves supplying the left ventricle enter the spinal cord from the left Anginal pain distributed over the right side may indicate involvement of the right side of the heart In patients with dextrocardia, angina may be referred almost exclusively to the right of the midline In some patients pain from the heart has been referred to the left upper or left lower quadrants in the abdomen, to the epigastrium or even to the teeth or sinuses

Travell[14] reported that anginal pain could be promptly alleviated by spraying the precordium with an ethyl chloride spray Rinzler[15] reviewed evidence that coronary occlusion may produce trigger areas in chest muscles from a "visceromotor" reflex similar to the spasm of abdominal musculature associated with acute inflammatory disease within the abdomen (e g , appendicitis) Spasm persisting in the thoracic musculature after the original pain in the heart has abated may also produce referred pain

SITE AND RADIATION OF ANGINA PECTORIS

A DISTRIBUTION OF ANGINAL PAIN



B CONVERGENCE OF VISCERAL AND SOMATIC AFFERENTS

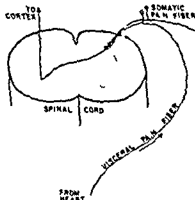


FIGURE 5 A Precordial pain or angina pectoris associated with myocardial ischemia usually seems most severe just beneath the sternum, but often radiates to more distant regions such as the left arm, right arm upper abdomen neck, *jaw* or *back* According to Rinzler 15 pressure on trigger zones (T) may produce the same kind of pain with a similar distribution. Blocking of the trigger areas with local anesthetics may alleviate angina pectoris.

B Both visceral and somatic afferent *nerves* probably impinge upon the same spinothalamic cells in the spinal cord. Thus one explanation of radiation of visceral pain is based on the subjective interpretation of impulses from visceral nerves as arising in somatic pain endings in the skin. (After Ruch.[12])

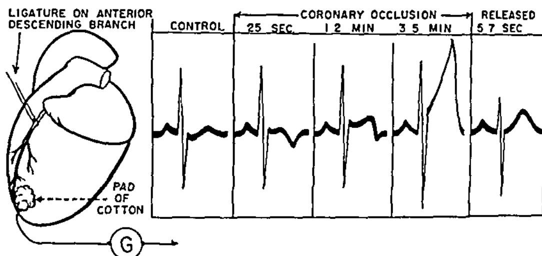


FIGURE 6 Experimental coronary obstruction rapidly produces dramatic changes in electrocardiograms recorded from cotton electrodes positioned over the ischemic area The initial change is a marked inversion of the T wave (at about 25 seconds) followed by elevation of the S T segment in about 1 5 minutes After 3 to 5 minutes the S T segment and T waves are both displaced upward These changes largely disappear in 5 to 7 seconds after release of the ligature

Trigger areas frequently develop in the pectoralis major, pectoralis minor and serratus anterior muscles of patients with persistent cardiac pain Stimulating the trigger areas by pressure or by inserting a needle produces pain which is referred to the same general areas as the original angina pectoris (Fig 5) Angina pectoris following acute myocardial infarction may be alleviated by local block of the trigger areas

Radiation of anginal pain may raise problems in the differential diagnosis of coronary atherosclerosis and diseases in other viscera such as the gallbladder [16] In patients with cholecystitis or peptic ulcer, angina may be ameliorated by eliminating the source of irritation in the gallbladder or the stomach but it rarely disappears Since most attacks of angina pectoris are transient differentiation between this condition and chronic cholecystitis or peptic ulcer should not be difficult It is important to keep in mind the fact that pain in these distant regions may be associated with disease of the coronary arteries

Even relatively slight intensities of visceral pain are peculiarly distressing and intolerable Not only is the pain subjectively disagreeable but stimulation of visceral afferents is prone to elicit powerful autonomic reflex activity often resulting in profuse sweating, epigastric uneasiness, bradycardia, hypotension and syncope Such attacks can be produced by mechanically stimulating the brachial artery [17] and also occur in the course of acute coronary occlusion

Electrocardiography in Angina Pectoris

Electrocardiograms from patients with angina pectoris rarely exhibit signs of myocardial ischemia because they are rarely obtained during a spontaneous attack In general, the electrocardiographic patterns between anginal attacks indicate only the underlying pathologic conditions For example many patients develop angina pectoris after myocardial infarction and residual signs of such myocardial damage may persist Similarly, electrocardiographic signs of left ventricular preponderance (see Chapter 15) are commonly encountered in patients with angina Acute coronary obstruction produces characteristic changes in electrocardiograms some of these changes are rarely observed during spontaneous attacks in patients but may be reproduced in experimental animals

Barley Ladue and York[18] temporarily obstructed the anterior descending branch of the left coronary artery in dogs and recorded the following sequence of events with exploring electrodes on the surface of hearts (Fig 6) Within 3 or 4 seconds after occlusion the T waves which had been positive became sharply inverted reaching maximal inversion in about 20 to 25 seconds Thereafter the inverted T deflections diminished in amplitude as the S-T segment became elevated and rounded with the convexity upward (Fig 6) The diastolic baseline (T-Q) was deflected in the opposite direction (see Fig 28 Chapter 15) After 3 to 5 minutes striking displacement of the S-T junction and upward peaking of T waves developed When the occlusion was released after 2 to 5 minutes S-T deviation and the large T waves vanished within 5 to 7 seconds indicating that the procedure did no *permanent damage to the myocardium* These striking electrocardiographic changes result from a functional change in the state of the affected myocardium rather than from demonstrable pathologic changes The changes in the S-T segment and T waves develop very rapidly and are easily demonstrable by experiments like those illustrated in Figure 6 because the *electrode is placed* directly on the site of myocardial ischemia They mimic the sequence of electrocardiographic alterations which develop *over a* much longer period of time following occlusion of coronary arteries in man (*vide infra*)

Diagnostic Tests for Angina Pectoris

STANDARD EXERCISE Angina pectoris is most commonly precipitated by physical exertion and standard exercise tests are frequently employed to induce precordial pain and electrocardiographic changes Master s two-step test[19 21] is probably the most familiar It consists of two steps each 9 in high which are climbed a prescribed number of times in exactly 1 5 minutes The number of steps ascended by a particular patient is determined from tables based on sex, age and weight An electrocardiogram is taken immediately after cessation of exercise and repeated after 3 and 8 minutes An abnormal response in the electrocardiogram consists of a depression of the S-T segment more than 0 5 mm below the isoelectric line or a positive T wave becoming flat or inverted A change from a previously inverted T wave to a flat or upright T wave is also classed as abnormal Other abnormal responses include multiple premature beats widening of the QRS complex deep Q waves prolongation of the P R interval or heart block These electrocardiographic signs are considered to indicate the presence of acute coronary insufficiency even though precordial pain is not induced

ANOXEMIA Although inhalation of gas mixtures containing 10 per cent oxygen has been widely used in the diagnosis of coronary insufficiency it is important to realize that oxygen saturation of the blood depends upon the partial pressure rather than the percentage concentration of the inspired air Thus breathing 10 per cent oxygen at sea level is equivalent to breathing 8 per cent oxygen at the altitude of Denver Colorado According to Patterson et al [22] an anoxemia test is positive when any *one* of the following is found

1 The arithmetic sum of the S-T deviations in all four leads (I II III and IV_F) is 3 mm or more

2 Partial or complete reversal *of the* direction of the T wave in lead I accompanied by an S-T deviation of 1 mm or more in this lead

3 Complete reversal of the direction of the T wave in lead IV_F regardless of any associated S T deviation in this lead

They considered development of pain during the test presumptive evidence of reduced coronary reserve even without significant changes in the electrocardiograms The level of arterial oxygen saturation at which the changes occur varies widely among *different* individuals[23] About 30

per cent of patients with angina pectoris have a negative response to the anoxemia test

ADMINISTRATION OF EPINEPHRINE Attacks of angina pectoris are frequently associated with strong emotions Raab[24] emphasized the fact that under the influence of sympathetic stimulation, oxygen consumption increases markedly and myocardial efficiency is diminished (see Chapter 8) Thus, myocardial hypoxia can occur without an increase in useful work of the heart The production of myocardial hypoxia by epinephrine or nor-epinephrine is aggravated if sclerotic coronary arteries fail to provide an adequate increase in flow

Levine[25] has employed the cautious administration of epinephrine (0 3 cc up to 1 0 cc of 1 1000 solution subcutaneously) to precipitate attacks of angina The test is somewhat dangerous, so nitroglycerin or amyl nitrite must be immediately available to relieve an attack

May[26] questioned the validity, the physiologic principles and the scientific accuracy of testing coronary "competence" by induced electrocardiographic changes He called attention to the fact that these types of induced stress are known to affect the electrocardiograms of normal individuals and exhausted and dying hearts do not necessarily exhibit such electrocardiographic changes In fact, the electrocardiographic response to gradually induced oxygen deficiency is greater in young persons than in older age groups Finally, most cases can be diagnosed without these tests, which may be dangerous or may occasionally be responsible for applying the label "cardiac patient" to a normal person

NITRITES A therapeutic test with nitrites may be both beneficial to the patient and helpful in arriving at a diagnosis However, the administration of amyl nitrite may produce misleading evidence of myocardial ischemia, apparently because the drop in arterial blood pressure may cause diminished coronary blood flow even in the presence of coronary vasodilatation[27] A similar mechanism is probably responsible for myocardial ischemia associated with hemorrhage[28] and a prominent cause of death under these conditions

BALLISTOCARDIOGRAPHY Ballistocardiographs record body movements which may be related to the force of the heart beat (see Chapter 12) In patients with myocardial ischemia the I wave diminishes or disappears and the configuration of the J wave is altered These changes are not specific for disease of the coronary arteries because they also occur in patients with myocarditis, metabolic diseases of the heart and heart failure[29]

A diagnosis of angina pectoris is not complete until the other sources of precordial pain are excluded and the etiology of myocardial ischemia has been determined as accurately as possible For example, similar precordial pain occurs with pulmonary hypertension[30] All of the conditions which may produce an abnormal load on the heart and restrict coronary blood flow should be included in the differential diagnosis The characteristic signs of many of these disease entities will be considered in subsequent chapters If the angina results from coronary atherosclerosis, acute massive myocardial infarction with sudden death could conceivably occur at any time

MYOCARDIAL INFARCTION

Acute Coronary Occlusion

Coronary arteries are most frequently occluded abruptly by thrombi formed in the lumen of the vessel Roughening of the endothelial surface over atheromatous plaques and encroachment on the arterial lumen produce eddy currents beyond the obstruction and contribute to thrombus formation (Fig 7*A*) Fragments of atheromatous plaques may break off and lodge at some point farther on Inflammatory processes in the arterial wall theoretically might play a role in some cases In recent years formation of hematomas within atheromatous plaques has received considerable attention (Fig 7*B*) Paterson[31] suggested that

hemorrhage into atheromatous plaques may predispose to thrombus formation in the lumen of the vessel Sudden expansion of the hematoma may occlude the arterial lumen without rupture of the intimal lining[3] Differentiating between such a condition and a mural thrombus at post mortem examination is difficult but the evidence for intramural hemorrhage is becoming more convincing Embolic obstruction of coronary arteries has been reported but is a rare phenomenon[33]

Infarction without Recent Coronary Occlusion

In one series of 143 patients dying in acute myocardial infarction 49 had no known recent coronary occlusion[34] The ventricles in three fourths of this puzzling group were hypertrophied to more than 50 per cent above normal The degree of coronary sclerosis was similar in all patients regardless of the occurrence of coronary occlusion However, occlusion usually produced transmural infarcts while the infarcts without occlusion were more frequently subendocardial Littman and Barr[35] reported 207 consecutive cases of acute coronary insufficiency of which 59 (28 5 per cent) were not attributed to coronary occlusion In these atypical cases the nature of the coronary insufficiency can be described only in general terms such as those considered in previous sections (see Chapter 8 and *General Causes of Myocardial Ischemia* above)

Changes in the Myocardium During Infarction

Experimental coronary ligation in the dog first produces an irregular area of cyanosis in the region supplied by the vessel Myocardium suddenly deprived of its blood supply contracts less vigorously, and within a

MECHANISMS OF CORONARY OCCLUSION

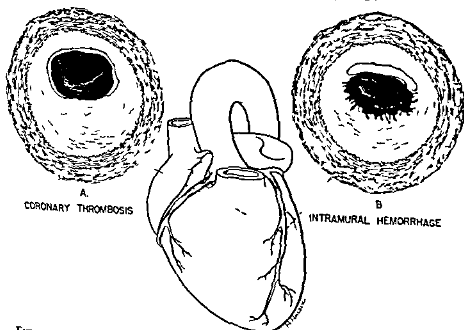


FIGURE 7 Two mechanisms have been postulated to account for acute coronary occlusion in patients with coronary atherosclerosis
A The most common cause is probably a thrombus which develops within the lumen of a sclerotic vessel.
B In some specimens coronary arteries appear to be occluded by hemorrhage into atherosclerotic plaques Such intramural hemorrhages are believed by some investigators to originate from capillaries growing into the atherosclerotic plaque from the lumen of the coronary artery rather than from vasa vasorum

minute loses so much contractile power that it stretches during isometric contraction, remains stretched during systole, and shortens during isometric relaxation [36] Oxygen tension, measured directly in the muscle decreases rapidly to less than 25 per cent of the baseline values In the border areas, the diminution in oxygen tension is less profound and beyond these borders there is no change [37] The border areas represent regions where the collateral circulation is not adequate for normal function, but is sufficient to maintain viability in the myocardium In the center of the ischemic tissue, congestion, hemorrhage and edema form in the connective tissue stroma, and cloudy swelling fatty degeneration and necrosis occur in the myocardial fibers Within two days fibroblasts concentrate in the borders of the infarct and by five days, a well defined zone of fibroblasts divides necrotic from living muscle After about three weeks, the infarcted area consists of a well formed scar of much smaller size than the original area of cyanosis, indicating that increased collateral circulation restored some of the border areas

The sequence of events during infarction in human hearts reconstructed by Mallory White and Salcedo-Salgar is similar to that described for the dog The principal differences are the delayed onset of fibroblast proliferation (four days) and delayed scar formation (two to three months) in man (see Bayley[38])

Diagnosis of Myocardial Infarction

Any particular patient with acute myocardial infarction may present either no definitive symptoms or, more frequently, a combination of a great many complaints The incidence of various symptoms in a group of cases studied by Bean[39] is indicated in Table 6 These signs and symptoms can be arranged in a functional grouping which provides a rational approach to responses of different patients (Table 7)

TABLE 6 INCIDENCE OF SIGNS AND SYMPTOMS OF MYOCARDIAL INFARCTION*

		FIRST ATTACK PER CENT	SECOND ATTACK PER CENT
1	Dyspnea	95	96
2	Enlarged heart	83	85
3	Weak heart sounds	85	82
4	Râles	83	82
5	Cyanosis	77	86
6	Cough	70	84
7	Pallor	69	79
8	Pain	75	66
9	Orthopnea	68	63
10	Sweating	60	60
11	Vomiting	59	59
12	Ankle edema	55	54
13	Shock	57	45
14	Restlessness	44	49
15	Tachycardia (rate over 100)	42	39
16	Systolic murmur	38	71
17	Cheyne-Stokes respiration	24	4
18	Ascites	26	33
19	Cloudy sensorium	26	23
20	Enlarged liver	18	27
21	Gallop rhythm	12	4
22	Prodromal phenomena	21	15
23	Bradycardia (rate below 80)	16	0
24	Angor animi	12	11
25	Pericardial friction rub	15	14
26	Pulsus alternans	9	8
27	Precordial hyperesthesia	8	10

* From Bean W B Infarction of the heart II Symptomatology of acute attack Ann Intern Med 11 2086-2108 1938

Pain with Myocardial Infarction The origin of pain in myocardial infarction is presumably the same as that in angina pectoris Pain from infarction is usually more severe and persists for longer periods of time, being unrelieved by cessation of physical exertion Indeed, many attacks occur when the patient is at rest or even asleep A wide variety of descriptive words are used by different patients to indicate the type of pain they experienced (Table 8) In general, these terms are the same as those used to describe anginal pain, to which about half of the patients have been subject prior to their first attack of acute myocardial infarction

TABLE 7 FUNCTIONAL GROUPING OF SIGNS AND SYMPTOMS OF MYOCARDIAL INFARCTION

I Pain
II Autonomic Effects

A. Pallor	E. Syncope
B. Sweating	F. Tachycardia
C. Vomiting	G. Shock
D. Bradycardia	H. Disturbed Sensorium

III Diminished Myocardial Contractility

A. Congestive Heart Failure

1. Left ventricular failure	2. Right ventricular failure
a. Dyspnea	a. Peripheral congestion
b. Orthopnea	b. Enlarged liver
c. Cough	c. Edema
	d. Cyanosis

B. Cardiac Signs

1. Weak heart tones	5. Ventricular enlargement
2. Gallop rhythm	6. Paradoxical pulsation
3. Systolic murmur	7. Pericardial friction rub
4. Pulsus alternans	8. ECG

TABLE 8 TYPES OF PAIN IN MYOCARDIAL INFARCTION*

	PER CENT
Crushing pressure	44
Squeezing constricting vise-like	29
Choking smothering suffocating	18
Sharp stabbing knife like	11
Sore aching dull	11
Excruciating	7
Burning	5

From Bean W B Infarction of the heart. II Symptomatology of acute attack. Ann. Intern Med 11 2086-108 1938

In some patients acute myocardial infarction may not be accompanied by any pain but there is disagreement concerning the frequency of this circumstance Bean[39] reported 28 per cent of attacks without pain while Kennedy[40] found only 4 per cent In reviewing the literature Pollard and Harvill[41] found the reported incidence of painless myocardial infarction to vary from 61 per cent to 4 per cent. The actual incidence of painless myocardial infarction probably lies somewhere between these figures but no value can be stated with confidence When myocardial infarction occurs without pain some combination of the other possible symptoms and signs can generally be discovered (Table 7) These 'substitution symptoms' are particularly important in the absence of the typical precordial pain

AUTONOMIC RESPONSES TO MYOCARDIAL INFARCTION *Syncope* Pallor sweating epigastric uneasiness and vomiting, bradycardia hypotension and syncope result from a powerful autonomic response initiated by a wide variety of stimuli including (*a*) powerful emotions (*b*) unpleasant sights (*c*) moderate venesections (*d*) vasodilating drugs (*e*) stimulation of visceral afferent nerves as in the carotid sinus syndrome, and (*f*) visceral pain A precipitous reduction of arterial blood pressure results primarily from a lowering of total peripheral resistance without a corresponding increase in cardiac output Bradycardia in the presence of arterial hypotension is an inappropriate autonomic response indicating the extent to which the regulatory controls have been unbalanced The bradycardia may be an important factor in the failure of the cardiac output to increase in the face of reduced total peripheral resistance In other words the compensatory mechanisms responsible for maintaining the arterial blood pressure are thrown out of balance by an overriding autonomic reflex response However, as soon as the stimulus is removed the normal equilibrium between peripheral resistance and cardiac output is rapidly restored Syncopal attacks of this sort generally occur when the individual is erect and are promptly terminated when the patient lies down If the patient is reclining the same stimuli rarely induce syncope In acute myocardial infarction the stimulus is very powerful and is not promptly relieved Severe hypotension may persist in reclining patients with coronary occlusion

Shock Shock is characterized by a progressive reduction in blood pressure due to persistent deficiency of cardiac output in spite of tachycardia and intense peripheral

vasoconstriction Thus, the principal deficiency is a reduction in stroke volume This condition is classified under autonomic responses in Table 7, in view of evidence that the diminished cardiac output is probably not caused solely by a disorder of myocardial contractility and the fact that many patients with extensive myocardial infarction fail to develop shock For these and other reasons, the fundamental disturbance in shock is more appropriately considered a disturbance of autonomic controls Despite a tremendous volume of research on the experimental forms of shock, the exact mechanisms remain controversial The extent to which diminished contractility and distensibility contribute to the picture is not known The factors which produce such a profound disturbance of autonomic or humoral mechanisms remain to be elucidated They must be very powerful because they override the compensatory mechanisms which normally maintain the equilibria in the cardiovascular system

It has been suggested that the fall in arterial blood pressure during shock from myocardial infarction is beneficial because it reduces the load on the ventricle This observation overlooks the drop in coronary perfusion pressure which accompanies any significant decrease in arterial blood pressure Indeed, myocardial infarction is sometimes precipitated by shock produced during surgery For this reason, it is imperative that the shock which accompanies acute myocardial infarction be combated as promptly and effectively as possible

Diminished Myocardial Contractility

When a portion of the left ventricular wall is suddenly deprived of its blood supply, the involved myocardium soon loses its ability to shorten during systole Its contractile power is so diminished that it becomes stretched as the remainder of the ventricular wall contracts Thus, the infarcted region not only fails to contribute to systolic ejection but places an added volume load on the remainder of the myocardial fibers Bulging of the infarcted region during systole is caused by the displacement of blood which would otherwise have been ejected into the aorta Thus, the myocardial fibers which are still actively contracting must increase their energy release and also shorten to a greater extent to make up for the bulging of the ischemic region Clearly the extent of effective compensation by the remaining myocardial fiber depends upon the location and size of the infarcted region Interruption of the blood supply to a large portion of the deep constrictor fibers in the left ventricle generally produces sudden death On the other hand, an infarct of similar size at the apex is more frequently survived The condition of the myocardium and the coronary arteries also plays an important role in the immediate survival of the patient The symptoms of diminished myocardial contractility due to myocardial infarction are the same as those of congestive heart failure from any cause (see Chapter 9)

There may be signs of left ventricular failure during and after acute infarction of the left ventricle Right ventricular failure may also develop following acute left ventricular myocardial infarction and lead to peripheral congestion, edema ascites, enlarged liver and cyanosis (see Chapter 9) However this must not be interpreted as an infarction in the right ventricular wall Although the right coronary artery is frequently involved in atherosclerotic processes isolated infarction of the right ventricular wall is very rare[42] Signs of right ventricular failure developing after myocardial infarction usually mean that left ventricular failure has imposed an increased load on the right ventricle presumably through pulmonary hypertension The right ventricular wall may occasionally be involved by extension of an infarct across the interventricular groove The relative rarity of right ventricular infarction suggests that the blood supply to the right ventricle is great in relation to its load, which is usually much less than that of the left ventricle

Auscultatory Signs

Although precordial pain and the peripheral vascular signs tend to dominate the clinical picture of myocardial infarction auscultatory examination of the heart may reveal a number of helpful clues

The heart sounds are often weak or muffled The cause of this change in heart sounds is not known The third heart sound often becomes audible near the apex producing a gallop rhythm (see Chapter 13) A systolic murmur is frequently heard and has been attributed to relative mitral insufficiency following dilatation of the left ventricle (see Fig 17 Chapter 13) Local regions of pericarditis over the infarcted area may produce a friction rub which is audible within the first two days after an infarction and persists or recurs over a period of four or five days

The arterial blood pressure is generally reduced below the level sustained before the infarction, particularly if the patient had been hypertensive For obscure reasons the blood pressure tends to remain low for a long time The force of left ventricular contraction may be reduced on every second cycle, so that the systolic pressure fluctuates 4 to 10 mm Hg on alternate beats This is called *mechanical alternans* and may be demonstrated during sphygmomanometry Only half of the pulses may pass under a cuff inflated to a pressure between the two systolic pressure levels. Premature contractions or short bouts of paroxysmal tachycardia are frequently encountered during the first few hours or days after infarction They may herald the development of ventricular fibrillation and sudden death

Roentgenography

Roentgenography frequently reveals an enlarged heart but it must be remembered that a majority of these patients had systemic arterial hypertension or organic heart disease before the infarction Fluoroscopy occasionally discloses a portion of the ventricular silhouette which bulges outward during systole This paradoxical pulsation corresponds to the bulging of the weakened myocardial wall described above Electrokymographic tracings may substantiate the reversal of pulsation [43] but rarely disclose a change which could not be recognized during fluoroscopy

Electrocardiographic Signs

Acute myocardial infarction produces sequential changes in the electrocardiographic patterns which are often the most obvious diagnostic signs In Chapter 15 changes in the configuration of the various electrocardiographic complexes were described in terms of alterations in the rate and course of depolarization and repolarization These principles should be utilized in visualizing the altered patterns occurring after myocardial infarction Since the electrocardiographic patterns change progressively following the attack it is important to obtain serial electrocardiograms at intervals dictated by the patient s progress The evolution of the electrocardiographic patterns during myocardial infarction is illustrated in Figure 8

Phase I If the infarcted region includes the epicardial surface ischemia of the affected myocardium apparently alters the process of repolarization The T waves in various leads become either sharply inverted or very tall and peaked depending upon the orientation of the electrodes in relation to the infarct The patterns depicted in Figure 8 represent records obtained from a unipolar electrode facing the infarcted region The changes in T waves are so transient that they are rarely recorded clinically [45] This initial phase of the sequence was first discovered following experimentally induced infarction in dogs (Fig 6) Frequently the rate of repolarization is sufficiently changed locally so that the S-T segment also is displaced generally in the same direction as the T wave (see Fig 6) The changes in S-T segment and T wave deflection in any particular lead depend

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near the center of the infarct becomes mechanically and electrically inactive The spread of excitation does not invade the inactive myocardial tissue which does not contribute to the QRS complex Electrodes facing the infarct register a prominent negative deflection because the waves of excitation spreading through distal regions of the heart are moving away from the electrode This negative potential appears early in the process of excitation and produces prominent Q waves in records from particular leads Pardee[46] noted early that Q waves with an amplitude greater than 25 per cent of the R wave occurred in lead III records taken from a substantial proportion of patients with clinical or pathologic evidence of myocardial infarction The Q waves become deeper as more and more myocardium in the center of the infarct dies At the same time the myocardium which has been injured either dies or recovers as collateral circulation is augmented so the S-T segment deviation tends to dwindle as the Q wave becomes more pronounced The T wave remains inverted indicating continued ischemia in the fringe around the dead myocardium The inverted sharply peaked T wave with an upward convexity of the S-T segment was called a coronary T wave by Pardee[47] and is now frequently referred to as the Pardee type of T wave

Phase II Over a period of *months* the ischemic myocardium either fully recovers or dies The inverted T waves may become upright leaving Q waves as the sole remaining sign of the previous infarction

If this sequence of electrocardiographic patterns appeared consistently in all patients with myocardial infarction diagnosis would be very simple Actually characteristic changes occur in only about two-thirds of patients In the remainder the typical patterns tend to be masked by such pre-existing conditions as bundle branch block ventricular pacemaker left heart strain or previous infarction A very wide variety of electrocardiographic changes is encountered owing to differences in the extent and location of the infarcted region[48] An intramural infarct produces no change in electrocardiograms for the same reason that a uniformly polarized cell produces no external potential (see Fig 6B Chapter 15) At the same time, a number of other conditions may be associated with electrocardiographic patterns which closely resemble those characteristic of infarction (see Fig 29 Chapter 15) For example right and left ventricular hypertrophy and strain may produce QRS-T patterns which can easily be confused with those of myocardial infarction[49-51] The reasons for the similar patterns resulting from different functional states are obvious since the electrocardiographic patterns change only because the course rate and extent of polarization and depolarization are affected In spite of its recognized limitations electrocardiographic interpretation is a valuable adjunct in the diagnosis of myocardial infarction By utilizing the various standard electrode positions one can determine the location and extent of most myocardial infarctions Sample electrocardiograms from two common types of infarction are illustrated schematically in Figure 9 An infarct on the anterolateral surface of the heart results from occlusion of the anterior descending branch of the left coronary artery A prominent Q wave develops in lead I the S-T segment is elevated and the T wave is deeply inverted A unipolar precordial electrode placed over the affected region produces a similar pattern illustrated in Figure 8D As the infarct heals the S-T segment returns to the baseline leaving a prominent Q wave and an inverted T wave in lead I This produces the well known Q_1T_1 pattern of anterior (or anterolateral) infarction

Conversely, an infarct on the posterior or diaphragmatic aspect of the heart usually results from occlusion of a posterior descending branch In this case the Q wave appears in lead III where the S-T segment is elevated and the T wave inverted As the infarct heals a Q_3T_3 pattern develops In

upon the size, location and orientation of the affected area in relation to the particular electrodes involved

Phase II As ischemia continues, the rate of repolarization becomes progressively slower This causes the T wave to reverse in direction At the same time, the extent of polarization or depolarization diminishes, which causes displacement of the S-T segment The T wave is deflected in a direction opposite to the deviation of the S-T segment, because the latter is a combined effect of an altered rate of repolarization (primary T wave changes) and changes in the extent of depolarization or repolarization (see the S-T segment shifts in Fig 8) These two effects have different time courses, and are generally attributed to two different degrees of myocardial dysfunction Probably the blood supply to the tissue at the periphery of the infarcted area is only slightly diminished because collateral channels of capillary size extend into this area from the normal tissue Deeper within the infarct, a greater degree of myocardial ischemia would be expected as the distance from normal vessels increases There is probably a gradient in the degree of ischemia from the normal tissue toward the central portion of the infarct where the myocardium will ultimately die and be replaced by connective tissue However, for the sake of convenience this ill defined shell of damaged myocardium is divided into two zones (*a*) a zone of ischemia which lies near the normal tissue and is believed to be responsible for the primary T wave changes, and (*b*) a zone of injury with an abnormal extent of polarization or depolarization producing S-T segment deviations (see Fig 8)

Phase III Eventually, the myocardium

ELECTROCARDIOGRAPHY OF MYOCARDIAL INFARCTION

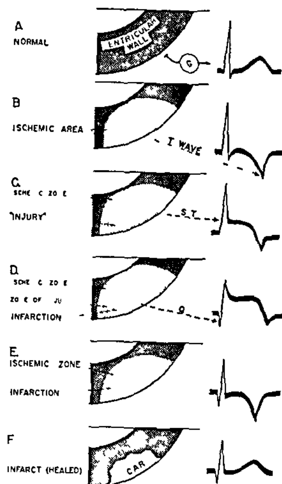


FIGURE 8 The sequence of electrocardiographic patterns recorded from unipolar electrodes over the site of a developing infarct is presented as reconstructed by Bayley [44]

A A normal electrocardiographic pattern recorded from a precordial electrode is illustrated for comparison

B Immediately after occlusion of a coronary artery the myocardium served by the vessel becomes ischemic A change in the rate of repolarization in the area produces a strongly inverted T wave (see also Fig 6)

C Within a short time myocardial hypoxia interferes with the repolarization process to the point that the affected myocardium fails to polarize to the normal extent Incomplete repolarization produces an injury current by the mechanism illustrated in Figure 28 Chapter 15 The S T segment assumes a different level than the T-Q segment this is generally described as a displacement of the S T segment

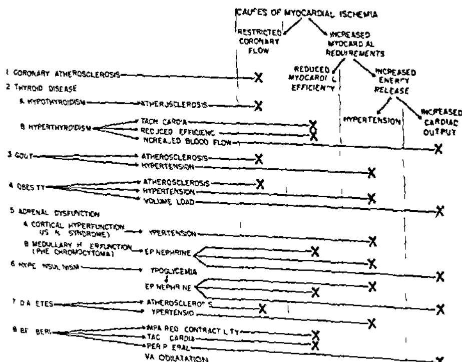
D Within the center of the ischemic region some of the myocardium dies and fails to contribute to the potentials during either systole or diastole Under these conditions a Q wave appears because the proximal tissue fails to balance the potentials in more distant regions where the wave of excitation is moving away from the electrode

E The myocardium in the zone of injury either dies or is incorporated in the ischemic zone so the injury current disappears and the S T segment returns to the baseline The ischemic zone persists as indicated by the sharply inverted T wave

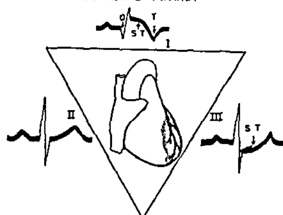
F In a healed infarct the ischemic zone is supplied by collateral vessels and returns to normal The only residual sign is the Q wave which is attributed to the presence of electrically inactive scar tissue.

severe atherosclerosis as well as systemic arterial hypertension Obesity is frequently accompanied by atherosclerosis and mild or moderate degrees of arterial hypertension with some potential increase in the volume load on the heart due to the prolifera tion of capillary beds into newly formed adipose tissue Systemic arterial hypertension is a prominent feature of adrenal cortical hyperfunction (Cushing's syndrome) Since epinephrine reduces myocardial efficiency and increases systemic arterial blood pressure and cardiac output excessive release of epinephrine (e g from *pheochromocytomas*) imposes a severe load on the heart which may seriously tax coronary blood flow and induce myocardial ischemia Similarly the hypoglycemia produced by excessive insulin in the blood appears to stimulate release of abnormally large amounts of epinephrine On the other hand diabetes is characteristically associated with severe atherosclerosis and some degree of systemic arterial hypertension In beriberi the heart enlarges very greatly and myocardial contractility diminishes, apparently as a result of impaired thiamine metabolism by heart muscle Tachycardia which also impairs myocardial efficiency is a prominent feature of the disease Finally, a severe volume load is imposed on the heart through extensive peripheral vasodilatation In a case reported recently[53] catheterization of a patient with beriberi disclosed a cardiac output of 16 1 l per minute oxygen consumption of 353 cc O per minute and and A-V oxygen difference of 2 2 cc O_2 Thus, the increase in cardiac output was not in proportion to the body s oxygen requirements as evidenced by the diminished A-V O_2 (see Chapter 8) Two hours after thiamine administration, the cardiac output was reduced to 12 l per minute the oxygen consumption increased to 415 cc per minute and the A-V oxygen difference was 3.45 cc. O_2 The sustained elevation of cardiac out

TABLE 9 CAUSES OF MYOCARDIAL ISCHEMIA IN METABOLIC DISEASES



LOCALIZATION OF MYOCARDIAL INFARCTION



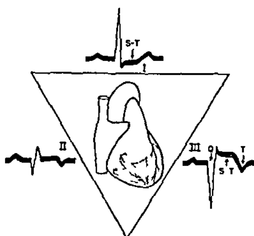


FIGURE 9 *A* An anterolateral infarct produced by occlusion of the anterior descending branch of the left coronary artery produces a fairly characteristic pattern In lead I a prominent Q wave appears with elevation of the *S-T* segment and inversion of the T wave This pattern resembles that presented in Figure *8D* During recovery the S-T segment returns to the baseline leaving a Q wave and an inverted T wave in lead I (the Q_1T_1 pattern) In lead *III the S-T segment is depressed and the T wave is* upright so the pattern reverts to normal more quickly in lead III than in lead I

B A posterior infarct produces a prominent Q wave in lead III with an elevated S-T segment and an inverted T wave During recovery this infarct produces the Q_3T_3 pattern

farction in different regions of the heart changes the patterns in the various leads in accordance with the principles discussed in Chapter 15 Additional details can be obtained from standard texts on electrocardiographic interpretation

Ballistocardiography

Proponents of ballistocardiography believe that certain "abnormal" changes in the configuration of ballistic patterns are useful in recognizing myocardial infarction For example, Moser et al [52] reported abnormal ballistocardiograms in approximately 80 per cent of patients with previous myocardial infarction In approximately 20 per cent, the records were normal and probably remained normal for years Several types of abnormal patterns were observed, including (*a*) diminution of the I wave, (*b*) a bizarre pattern with small deflections, (*c*) notched J waves, (*d*) prominent H wave and a few others Lacking experience with the method, I am not in a position to judge the reliability of ballistocardiographic interpretation

MYOCARDIAL ISCHEMIA IN CERTAIN METABOLIC DISEASES

The basic causes of myocardial ischemia involve restricted coronary blood flow, and *increased myocardial requirements due to* (*a*) diminished myocardial efficiency or (*b*) increased myocardial energy *release* (*e g*, from arterial hypertension or increased output) *As* indicated in *Table 9*, a wide variety of metabolic diseases are potential causes of myocardial ischemia *through one or* both of these mechanisms This type of analysis reveals the fallacy of regarding myocardial ischemia solely in terms of restricted coronary blood flow from coronary atherosclerosis For example, hypothyroidism not only causes cardiac enlargement (myxedema heart), apparently involving impaired myocardial metabolism, but also fosters the development of atherosclerosis Hyperthyroidism not only interferes with myocardial efficiency by inducing persistent tachycardia and by direct metabolic effects on the myocardium, but also imposes a sustained volume load on the heart to support the increased level of metabolism These effects are discussed in greater detail below Patients with gout often develop unusually

that of normal individuals performing the same task

In young persons the heart may compensate for this excessive load but in older individuals, cardiovascular reserve may become exhausted and heart failure supervenes Clearly a degree of coronary sclerosis which would not produce symptoms in an otherwise normal individual may produce myocardial ischemia on effort in the presence of hyperthyroidism Recognizing the nature of the disease a high incidence of angina pectoris in older patients with this condition is not surprising Atrial fibrillation also is quite common presumably because irritability of the myocardium is increased

It is unnecessary to postulate that increased thyroid hormone directly induces *organic cardiac* disease The excessive load on the heart accentuates the effects of other disease processes and this is sufficient to explain the clinical manifestations of the disease

Signs and symptoms of hyperthyroidism Thyrotoxicosis is a systemic disease which produces a diversity of signs and symptoms The condition can develop at any age but most commonly appears between 20 and 40 years Characteristic symptoms include nervousness and irritability warm moist skin fine tremor of the extended hands palpitation and intolerance of a warm environment If exophthalmus is present, the expression is slightly staring because the palpebral fissures are widened and blinking of the eyes is infrequent Diarrhea and weight loss in spite of good appetite are common The early manifestations of the disease are difficult to distinguish from psychosomatic disorders Exophthalmus is absent in a large percentage of cases and is apparently not caused by direct action of the thyroid hormone because it cannot be reproduced by administering the substance to man or to animals Protrusion of the eye balls results from expansion of both fat and muscle in the retrobulbar portion of the orbit

Cardiovascular manifestations of hyperthyroidism The heart rate is rapid (e g from 90 to 160 or more per minute) and the pulse is forceful resembling the water-hammer pulse of aortic insufficiency (see Chapter 18) The rhythm is usually regular, although premature contractions may occur Extreme irregularity of the cardiac rhythm (atrial fibrillation) discovered unexpectedly should stimulate a search for signs of hyperthyroidism because it is often the first clue to the condition The atrial fibrillation may occur in paroxysms of varying duration

In view of the increased cardiac output peripheral vasodilatation and bounding pulse, the systolic pressure should be elevated and the diastolic pressure depressed to produce an increased pulse pressure However the pulse pressure often is not beyond the limits of normal (see Fig 2 Chapter 20)

The heart is generally enlarged to a degree dependent upon the severity and duration of the thyrotoxicosis The precordial cardiac impulse is forceful and diffuse The first sound is usually loud at the apex. A systolic murmur with maximum intensity in the pulmonary area is commonly found and may result from the rush of blood through the pulmonary artery (see Fig 16 Chapter 15) A definite presystolic murmur is sometimes heard and a prominent third heart sound may result from rapid ventricular filling Such patients with a loud snapping first heart sound prominent pulmonary second sound and presystolic murmur must be carefully distinguished from those with rheumatic mitral valvular stenosis (see Chapter 18) This is particularly important since rheumatic valvular heart disease may occur in patients with thyrotoxicosis However adequate therapy of hyperthyroidism eliminates the abnormal sounds and murmurs due to this cause

The blood volume tends to increase with hyperthyroidism and the accumulation of blood in the pulmonary circuit tends to diminish vital capacity and stimulate reflex dyspnea particularly during exertion (see Fig 4 Chapter 9)

Fluoroscopic examination of the heart

put in both beriberi and hyperthyroidism is equivalent to uninterrupted physical exercise continuing day and night so far as the heart is concerned. The functional effects of thyroid dysfunction are discussed in greater detail for reasons set forth below.

Thyroid Dysfunction

Abnormality of thyroid activity has been selected for particular attention in this section for two reasons: (*a*) Excessive thyroid secretion impairs myocardial efficiency while greatly increasing the load on the heart. (*b*) In recent years considerable attention has been directed toward the induction of hypothyroidism to provide symptomatic relief of patients with advanced heart disease, particularly those diseases which produce myocardial ischemia.

HYPERTHYROIDISM. *The precise chemical structure of the hormone released by the* thyroid gland is not known, although it certainly contains amino acids in which iodine is incorporated. Functional disturbances resulting from deficiency in the thyroid hormone can be corrected by the administration of thyroxin, thyroid extracts, thyroglobulin, or iodinated casein. One function of the thyroid hormone is to accelerate oxidative processes in many tissues, since it increases the oxygen consumption of excised pieces of heart, liver, kidney and brain.[54] The metabolism of other substances such as carbohydrate, fat, electrolytes, and vitamins is influenced primarily by the generalized increase in metabolic rate.

The effects of thyroid hormone on the heart rate. Priestley et al[55] administered thyroxin to rabbits and dogs for several days. Even when the hearts of these animals were excised and used in heart-lung preparations, *the heart rates were significantly faster than* hearts from normal animals. A heart transplanted into the neck of a donor animal developed tachycardia when thyroxin was administered to the host. Thyroxin administered to *fragments of embryonic hearts* excised before nerve elements appeared, produced progressive acceleration of the heart and occasional irregularities in rhythm. The fragments also ceased pulsating sooner than the controls.[56] This was *attributed to* exhaustion of the muscle cells and accumulation of metabolic waste products. Irrigation of the specimen with Tyrode solution to wash away metabolic products restored *pulsation at rapid rates.* Tachycardia is also induced by thyroxin administered to dogs with denervated hearts.[57] The evidence seems clear that the tachycardia from excess thyroid hormone represents a direct effect on the pacemaker activity of the myocardium.

One important aspect of the action of thyroid hormone *is the reduction in the efficiency* with which work is performed, both by skeletal muscle and by myocardium. The oxygen consumption at rest is elevated (increased basal metabolic rate), and a given *quantity of muscular work causes an abnormally* great increase in oxygen consumption, peripheral blood flow, cardiac output and heart rate. Perhaps thyroxin inhibits certain enzymes involved in the anaerobic synthesis of high-energy phosphate bonds, and the alternative aerobic reactions increase the oxygen consumption[58] and diminish efficiency. Be that as it may, hyperthyroidism imposes a heavy load on the myocardium which must put out greater quantities of useful work to supply the augmented *metabolic requirements of the body while* the efficiency of its contraction is diminished by tachycardia and by direct action of thyroid hormone on the myocardial fibers.

Functional effects of hyperthyroidism. The circulatory *response to hyperthyroidism resembles* that of a normal person to strenuous exercise.[59] The cardiac impulse is diffuse and forceful, the heart is accelerated, the pulse pressure is widened and the skin capillaries *are dilated.* When the metabolic rate of a resting patient is 35 per cent above normal, the cardiovascular response is equivalent to that of a normal individual continuously performing moderate exercise day and night. When a patient with hyperthyroidism undertakes physical exertion, the circulatory reaction is extravagant when compared to

to improve coronary blood supply) The ultimate role of such therapy remains undetermined even though it appears to have some place in the armamentarium Obviously such methods are inherently undesirable since they are drastic steps used to improve rather hopeless conditions The hope of the future lies in the development of methods for preventing atherosclerosis and organic heart disease at their inception

SUMMARY

Myocardial ischemia occurs whenever the coronary blood flow is insufficient in relation to the oxygen requirements of the myocardium Many types of cardiac disease simultaneously increase the requirements for myocardial energy release while interfering with delivery of oxygen to the myocardium For this reason myocardial ischemia can be an important limitation on cardiac reserve in virtually all types of cardiac disease

Direct interference with coronary blood flow most commonly results from coronary atherosclerosis which develops *to a* significant degree in more than 70 per cent of men over 50 years of age Moderate coronary sclerosis can be compensated by peripheral vasodilatation in the terminal coronary arterial tree and by expansion of collateral vessels Progressively increasing coronary obstruction usually affects several branches of the coronary tree and the coronary flow reserve is depleted Characteristic pain in the precordium (angina pectoris) often radiating to other regions occurs in some patients with coronary atherosclerosis during exertion and disappears quite promptly with rest Spasm of the coronary vessels probably plays an important role in the production of this type of precordial pain

Gradual occlusion of coronary vessels provides time for collateral circulation to develop and destruction of myocardial tissue is thereby avoided However a sudden occlusion of a coronary artery produces both dysfunction and death of myocardium deprived of its blood supply A surprisingly large proportion of hearts showing infarction at postmortem examination have no obvious signs of recent coronary occlusion The principal signs and symptoms of myocardial infarction can be considered in terms of (*a*) intense radiating *precordial pain* (*b*) severe autonomic responses (*c*) heart failure from diminished ventricular contractility, (*d*) changes in heart sounds and blood pressure (*e*) roentgenographic findings and (*f*) electrocardiographic signs Although the electrocardiographic interpretation of signs of myocardial infarction is somewhat empirical serial records coupled with careful clinical studies usually indicate the diagnosis Since the electrocardiographic changes are rather non-specific, a number of other conditions can produce similar patterns (e g ventricular strain patterns) For this reason, the diagnosis must depend upon sound judgment applied to the total clinical picture

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reveals large and forceful movements of the ventricular borders, due to increased cardiac output The pulmonary artery is usually *prominent and its pulsations are increased* The area of the cardiac silhouette is not necessarily enlarged in young persons

Electrocardiograms are usually within normal limits unless there is associated *cardiovascular disease, atrial fibrillation* or ventricular hypertrophy

HYPOTHYROIDISM Hypothyroidism usually results from either spontaneous atrophy or surgical excision of thyroid tissue The principal signs are weakness, fatigability, somnolence, slowed mental reactions, poor appetite and loss of weight,[54] puffiness of the skin (particularly around the eyes), diminished perspiration and generalized loss of hair These signs and symptoms develop insidiously over a period of many years As the clinical course progresses, the puffiness around the eyes spreads to include the entire body (myxedema), mental retardation becomes severe, and the voice is hoarse and low pitched The heart rate is slow, and the P and T waves have low voltage Cardiac enlargement, principally dilatation, develops during the final stages in the disease The cardiac silhouette closely resembles that produced by pericardial effusion In many patients, fluid in the pericardial sac, superimposed upon cardiac enlargement, contributes to the large cardiac silhouette *Atherosclerosis is prone to develop to* extreme degrees in patients with severe hypothyroidism, and may lead to myocardial infarction Myxedema is a rare condition, and current interest in the subject is largely directed toward the therapeutic induction of hypothyroidism to ameliorate intractable angina pectoris

Therapeutic induction of hypothyroidism in intractable heart disease In patients with heart failure or with a coronary blood supply in precarious balance with the myocardium s oxygen consumption, the maximal cardiac output is barely adequate to provide for the body's oxygen consumption at rest Theoretically, reducing the oxygen consumption of the body and of the heart would correspond to increasing the reserve capacity of the heart A patient confined to bed for extended periods because of congestive heart failure, or by agonizing attacks of angina pectoris at rest or on the mildest exertion, should derive benefit from a subnormal metabolic rate On this basis, total thyroidectomy was proposed in 1933 for the treatment of carefully selected patients with persistent congestive failure and severe angina pectoris[60] Parsons and Purks[61] reported on a survey of the results of this type of therapy in 1937 and concluded that there was "slightly more than a 50 per cent chance of satisfactory improvement in cases with congestive heart failure and somewhat better than 75 per cent satisfactory results in angina pectoris' Nonetheless, Levine[25] no longer recommends total thyroidectomy for either angina pectoris or congestive failure The sequelae of a mild myxedematous state detracted from the results and the symptoms tended to recur after variable periods of improvement

Thiourea is not suitable for inducing hypothyroidism because its action is very unpredictable when the metabolic rate is normal[62] *Very large doses must be used to* depress the metabolic rate below normal, it must be used indefinitely and dangerous reactions can occur at any time

Thyroid tissue can be permanently destroyed *by radioiodine*[62 65] *Blumgart*[67] has administered I^{131} to invalids unable to undertake more than slight effort without experiencing angina pectoris or congestive failure The clinical course of these patients was stationary or gradually downhill during the months prior to treatment In general, one-third of the patients have shown rather remarkable improvement, in another third the improvement has been definitely worth while, in another third no worthwhile improvement was achieved These patients were intractable cardiac cripples ordinarily *not considered for surgery* (sympathectomy, posterior rhizotomy and pericoronary neurectomy, and surgical techniques designed

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interest in acute non-specific myocarditis as a clinical diagnosis Inflammatory lesions in the heart from many different disease entities may produce signs closely simulating those of acute rheumatic fever

In 1941 Saphir[2,3] reviewed the subject of myocarditis expressing his belief that a more concerted effort by the clinicians and the pathologists would bridge the gap between the abundance of anatomic changes in the myocardium and their apparent clinical insignificance He presented an extensive review of the literature along with 240 patients with inflammatory lesions in the myocardium from 5626 autopsy reports Pathologic evidence of myocarditis was associated with a wide variety of acute infectious diseases and chronic illnesses including duodenal ulcers ulcerative colitis, carcinoma bronchiectasis tuberculosis, and congenital cardiac anomalies Interest in myocarditis was unquestionably aroused and the list of possible etiologic factors now embraces an extensive array of disease processes Changes in electrocardiographic patterns observed during systemic diseases have contributed to the expanding number of clinical syndromes which are frequently or rarely associated with myocarditis Candel and Wheelock[4] concluded that (a) electrocardiographic changes during acute or chronic infections reported in the literature are evidence of acute inflammatory processes involving the myocardium and (b) clinicians discover the condition even more frequently than the pathologist but diagnose it rarely because the term myocarditis has fallen into profound disrepute This statement was made in 1945 and since that time clinical reports on patients with evidence of myocarditis have continued to pour in. However no specific therapy has been proposed for acute non-specific myocarditis Under these conditions an accurate diagnosis of the condition provides a basis for prognosis supportive therapy professional pride and academic interest

Since antibiotic prophylaxis has been developed during a period when inflammatory lesions of the heart are being recognized very frequently clinicians are rather suddenly faced with the necessity of distinguishing acute rheumatic carditis from non-specific myocarditis with its diverse etiology, variable symptoms and vague signs Thus the importance of early and accurate diagnosis of the initial stages of rheumatic carditis places a heavy responsibility on physicians attending such patients Unfortunately, the signs and symptoms of acute rheumatic fever are also frequently vague and widely variable Two attacks in the same patient may produce entirely different responses Not all patients with acute rheumatic fever develop permanent damage to the heart or valves Scherf and Boyd[5] asserted their belief that virtually *everyone* develops inflammatory myocardial foci associated with acute infectious diseases on some occasion during a *lifetime* Clearly there is no justification for proposing extended prophylactic administration of antibiotics to everyone who develops signs of myocarditis or to restrict it to patients with all the classic signs of acute rheumatic carditis There is probably no field of medicine in which good judgment will be more essential than in the handling of patients with myocarditis until methods of diagnosis have been improved and the usefulness, deficiencies and dangers of prophylaxis have been established

ACUTE RHEUMATIC FEVER

The pathology etiology and extracardiac symptomatology of rheumatic fever are considered with reference to the general problems of diagnosis Recognition of acute rheumatic fever depends in part upon the criteria which delineate that entity

Definition of Acute Rheumatic Fever

Acute rheumatic fever is a general systemic disease characterized by widely disseminated focal and diffuse inflammatory reactions in connective tissue or various other tissues of the body frequently developing between one and three weeks after an-

Chapter 17

Myocarditis

In recent years the medical community has been faced with a problem of unparalleled magnitude in detecting and caring for patients with signs and symptoms of myocarditis Consider for a moment the sequence of events which led to this circumstance Fifteen or 20 years ago the death certificate of almost every elderly patient included the diagnosis of "chronic myocarditis" Since signs of inflammation and fibrosis in the heart are caused by a tremendous variety of conditions, city and state health departments became reluctant to accept "chronic myocarditis" as the cause of death, and with good reason Pathologists urged that this term be reserved for cases with evidence of primary inflammation of the myocardium Myocarditis then became a rare clinical diagnosis, almost a synonym for acute rheumatic carditis

In patients with the characteristic signs and symptoms of acute rheumatic fever, diagnosis was not difficult, but treatment was not particularly successful, it consisted of (*a*) supportive therapy during the acute attack (mainly salicylates and bed rest), and (*b*) futile attempts to prevent recurrent attacks or permanent damage to the valves of the heart

In 1940, Sosman[1] clearly expressed a widely accepted attitude of that period, as follows "There is little of therapeutic value *in the earlier diagnosis of mitral stenosis* as there would be in the early diagnosis of cancer or of pulmonary tuberculosis The treatment would not be any different nor would it presumably have any different effect The value in such studies must lie therefore in the difference in prognosis, with a possible change in our ideas as to the latent or inactive period in potential heart disease—that period between the first infection with rheumatic fever and the onset of symptoms or the discovery of physical signs of acquired valvular heart disease"

The "batting average" in diagnosing the early stages of acute rheumatic fever has not been particularly good As a matter of fact, rheumatic heart disease in 40 per cent of patients is first recognized only after permanent damage to the valves has produced *clinical manifestations* In other words, the original attacks of acute rheumatic fever must have been unimpressive or ignored The nature of the infectious processes, the signs and symptoms, and the course of the acute phases of the disease in this large group of patients are subject to controversy So long as there was no treatment which would ameliorate or prevent recurrent attacks, failure to diagnose the initial attack of rheumatic carditis made little *difference* in the course of the patient's subsequent illness Under those conditions, an attending physician felt no serious qualms of conscience when his first diagnosis of rheumatic heart disease came only after the valves were scarred and deformed

In recent years, the development of antibiotics has at last provided effective prophylaxis against recurrent attacks of acute rheumatic fever Prevention of recurrences should greatly diminish the likelihood of *permanent valvular damage* but requires prolonged administration of antibiotic agents For many reasons programs of antibiotic prophylaxis must not be *initiated in*discriminately so the accurate diagnosis of initial attacks of acute rheumatic fever has become exceedingly important Ironically, the recognition of acute rheumatic fever has been seriously complicated by resurgent

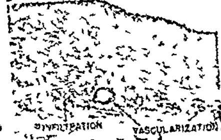
(see Fig 1, Chapter 1) this widespread involvement has been explained as a direct extension of the process from one ring to another.[7] Swift[8] postulated that the mitral and aortic valves more frequently became deformed because of the greater "functional trauma" to which they are subjected. He presented observations on one fever free patient who succumbed to an anesthetic on the nineteenth day of an apparently mild

ACUTE RHEUMATIC CARDITIS

A. PERICARDITIS



B VALVULITIS



C. MYOCARDIAL DEGENERATION



D ASCHOFF NODULES





FIGURE 1 A Pericarditis of extremely severe degree is illustrated by a specimen from a patient with fa acute pancarditis. In the average attack of acute rheumatic fever pericarditis appears to be a transient ph nomenon as evidenced by evanescent friction rubs and precordial pain.

B The valve cusps exhibit inflammatory reactions as evidenced by infiltrated leukocytes and vasculariza by the proliferation of blood vessels

C Degeneration of myocardial fibers is generally postulated but is rarely demonstrable as clearly as indica in the photomicrograph above No doubt functional changes in the myocardium occur without such obv histologic evidence

D Aschoff nodules in the myocardium are generally regarded as a pathognomonic sign of rheumatic fe The typical nodule consists of a perivascular infiltration with leukocytes including multinucleated giant c (Aschoff cells) Healing of such a nodule usually produces triangular fibrous scars surrounding blood vessel various portions of the heart walls (These photomicrographs were obtained through the courtesy of Profe Stuart Lippincott, Chairman of the Department of Pathology University of Washington Seattle)

infection involving group A hemolytic streptococci The inflammatory process is more obvious when localized in the heart, joints, and central nervous system, but it may also affect skeletal muscle, synovial membranes in general, blood vessels, lungs, gastro-intestinal tract, kidneys, etc

Pathologic Manifestations

The initial phases of myocarditis consist of inflammation and edema of the connective tissue stroma and intense eosin staining of the gelatinous ground substance between the collagenous fibers Later a homogeneous, waxy appearance of the collagen bundles becomes so marked that individual fibers cannot be identified This modified collagenous material superficially resembles fibrin A "proliferative" reaction ensues, consisting of either diffuse accumulations of cells, particularly in the vicinity of blood vessels or localized "granulomata" (Aschoff bodies) (Fig 1*D*) Round cells, macrophages, fibroblasts and multinucleated giant cells accumulate in focal lesions Typical giant cells have irregular outlines slight basophilic staining of the cytoplasm, and two to seven round or oval nuclei near the center of the cell, often arranged like a fan (Fig 1) Around the periphery of such lesions is an investment of polymorphonuclear leukocytes, lymphocytes plasma cells fibroblasts and occasional eosinophils As healing progresses, this inflammatory process is replaced by spindle-shaped or triangular scars located between muscle layers and near blood vessels

Inflammatory reactions also occur in other tissues Subcutaneous nodules, varying in size from 1 mm to 2 cm in diameter develop predominately over bony prominences They develop rapidly, usually disappear quickly and may be overlooked Microscopically, these nodules are not identical with the focal processes in the myocardium Subcutaneous lesions consist of aggregations of similar cells, but necrosis often develops *in the center of the lesion* Similar diffuse and local inflammatory reactions occur in many tissues including tendons, skeletal muscles joints serous cavities in general, and the adventitia of arteries Histologic evidence of meningo-encephalitis in patients with chorea has been reported During any particular attack, the pathologic changes may be localized in virtually any combination of the sites indicated above Thus, acute rheumatic fever is truly a systemic disease It affects primarily the supporting structures of the body, collagen and elastica Despite the wide spread distribution of the lesions, most patients recover and little residual damage to vital organs persists, except in the valves of the heart If valvular damage were not so frequent, this condition would be of no greater concern to cardiologists than is the non-specific myocarditis associated with a tremendous number of other acute and chronic diseases (*vide infra*)

Acute Rheumatic Valvulitis

Since the first attack of acute rheumatic fever is rarely fatal, pathologic changes during the typical initial attacks are not well established Available descriptions of the initial pathology in rheumatic endocarditis and valvulitis are based on postmortem studies of patients overwhelmed by rheumatic attacks or of fortuitously discovered endocardial inflammatory processes in accident victims In neither instance can one be certain that the individuals would have ultimately developed typical rheumatic valvular heart disease Until rheumatic valvular lesions can be reproduced experimentally, the reconstructed sequence of events must be accepted with some reservations

Gross and Friedberg[6] concluded that the valve rings were the first portion of the valves to be involved in the rheumatic process In patients who were believed to have succumbed during their first attack, the valve rings were the most common site of inflammatory reactions and in most cases *all four valve rings* were involved Since the valve rings are closely related anatomically

micro-organisms cannot be isolated from the blood stream heart or joints of patients with this disease

Streptococcal Infections

Since 1930 and particularly during World War II an association between recrudescence of rheumatic fever and infection with certain strains of hemolytic streptococci (in the group A of Lancefield) has been established For example acute rheumatic fever in army camps accompanied epidemics of streptococcal sore throats By eliminating streptococci from the nasopharynx in a group of susceptible individuals the rate of rheumatic fever attacks can be greatly reduced Many different types of hemolytic streptococci can be identified on the basis of immunologically distinct proteins in the bacterial cells None of these types is specific for acute rheumatic fever Certain strains of the organism produce substances which may be detected by the antibody responses in the host For example most strains of group A streptococci growing in cultures produce a substance called streptolysin O capable of causing lysis of rabbit erythrocytes Among individuals infected with streptococci some 90 percent produce an antibody (antistreptolysin O) at some time in the course of the disease However most individuals with streptococcal infections do not develop acute rheumatic fever

Coburn[10] contended that all attacks of rheumatic fever must be preceded by an infection with hemolytic streptococci by two or three weeks However the reported incidence of rheumatic attacks without clinical or laboratory evidence of streptococcal infection have been as high as 37 per cent[11] The apparent failure of antibiotics effective against streptococci to alter the course of an attack of rheumatic fever when administered after its onset is further evidence that the presence of live streptococci is not essential to the progress of pathologic changes Copeman[12] reported attacks of rheumatic fever precipitated by malaria dysentery and sand fly fever in North Africa Trauma cold dampness excessive fatigue and even psychic trauma have been incriminated

Hyaluronidase

Many strains of hemolytic streptococci produce a substance called hyaluronidase which can liquefy the gelatinous ground substance in the spaces between collagenous fibers in connective tissues (see Fig 6 Chapter 9) Since collagenous connective tissue is a prominent site of rheumatic activity, hyaluronidase was considered an important link between streptococcal infections and rheumatic manifestations Indeed dye injected into the skin does spread more rapidly in patients with acute rheumatic fever than in normal subjects[13 14] Salicylates which inhibit the effects of hyaluronidase also ameliorate signs of rheumatic activity However the correlation between hyaluronidase production pathogenicity of organisms and attacks of rheumatic fever has been rather poor and interest in this concept is waning

Immunologic Sensitization

It is well established that widespread tissue and vascular lesions occur during the height of an allergic reaction (e g sensitization to horse serum) For this reason great interest is currently directed toward immunologic reactions in the etiology of rheumatic fever Evidence has been presented that individuals who develop post streptococcal complications (e g rheumatic fever) tend to form larger amounts of various antibodies than do individuals who recover from the infection without complications In other words exaggerated antibody responses to streptococcal infections are believed to characterize individuals who are susceptible to rheumatic fever Lesions in the skin joints and heart superficially resembling rheumatic inflammatory reactions have been produced experimentally by a bewildering array of injected antigens including various types of living and dead bacteria or their products foreign serum egg albumin and even the animal s own

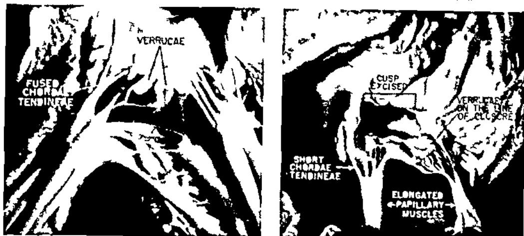


FIGURE 2 Some effects of acute rheumatic valvulitis on the mitral and tricuspid valves are indicated by a specimen from a patient who expired in the course of her initial attack

A, The mitral valve edges are greatly thickened with verrucae extending along filamentous chorade tendineae Some of the chordae tendineae are fused together All the chordae tendineae appear shorter and thicker than normal and the papillary muscles are unusually long but at least part of this relation could have antedated the inflammatory process The mitral orifice was only slightly diminished in area

B In the same patient a row of verrucae up to 3 mm thick developed along the line of valve closure on all tricuspid valve cusps The short thick chordae tendineae are also associated with elongated papillary muscles These diseased valves should be compared with the delicate flexible normal valves and chordae tendineae illustrated in Figure 5 Chapter 13 (This specimen is presented through the courtesy of Dr S A Creighton pathologist Children s Orthopedic Hospital Seattle Washington)

initial attack The aortic and mitral valves were edematous and infiltrated with mononuclear cells One small verrucous lesion with a very small necrotic focus underneath was found on the aortic valve At later stages, the valve leaflets become thickened and are no longer transparent Rows of gray or yellow wartlike vegetations develop along the line of closure of the aortic and mitral valves (Fig 2) The valve edges be-become thick, and newly formed blood vessels grow into the leaflets from the periphery The structure and function of the valves frequently become essentially normal after initial attacks of rheumatic fever Valvular deformities usually occur after repeated inflammatory assaults or protracted severe attacks of rheumatic fever

During the healing process, the inflammatory lesions are replaced by fibrous tissue Shrinkage of the collagen fibers usually causes shortening and retraction of the affected cusps The chordae tendineae of the atrioventricular valves become shortened and fused, drawing the valve edges toward the papillary muscles Fusion between the valve leaflets begins at the commissures and extends toward the center of the valve ring As a result, the flexible mitral valve leaflets are finally converted into a rigid funnel with a narrow orifice held deep within the left ventricular cavity by the shortened, fused chordae tendineae The semilunar valve leaflets are also thickened and shortened, with their edges rolled outward, and fusion of the commissures between the valve cusps restricts the valve orifices Various types of valvular deformities and their functional effects are discussed in Chapter 18

ETIOLOGY OF ACUTE RHEUMATIC FEVER

The nature and origin of rheumatic fever remain controversial Recently, Waksman[9] reviewed the subject and included an extensive bibliographic citation Before 1900, a wide variety of micro-organisms were cultured from patients with rheumatic fever It is now widely accepted that the causative

tacly rigid criteria for controlled investigation have demonstrable value when applied to groups of patients, but they are no substitute for clinical judgment in the care of an individual patient However the classification of signs and symptoms proposed by Jones forms a convenient organization for a discussion of this complex disease entity

Major Manifestations

CARDITIS In the proper setting the development of significant cardiac murmurs pericardial friction rub cardiac enlargement alterations in electrocardiographic patterns and congestive heart failure represents evidence of active carditis The clinical signs of carditis will be considered in more detail in a subsequent section

ARTHRALGIA The rapid development of painful joints which are tender warm swollen and red is generally considered a classic sign of rheumatic fever The arthritic process generally involves more than one joint migrating from one to another over a varying period of time The pain is sufficient to limit mobility of the affected joints and should be distinguished from myositis or vague muscular pains Although there is reason to believe that myositis may occur with acute rheumatic fever the symptoms are so non-specific that their significance is difficult to evaluate According to Jones transient mild polyarthritis without other diagnostic features of acute rheumatic fever is not significant unless the patient is a likely candidate for the disease on the basis of known contact with hemolytic streptococci

CHOREA The development of chorea is frequently heralded by personality changes For example a lively obedient good natured child may become sulky irritable and inattentive Awkwardness and frequent emotional upsets are prone to occur Finally irregular, incoordinated jerks and apparently purposeless movements appear The

CLINICAL MANIFESTATIONS OF ACUTE RHEUMATIC FEVER

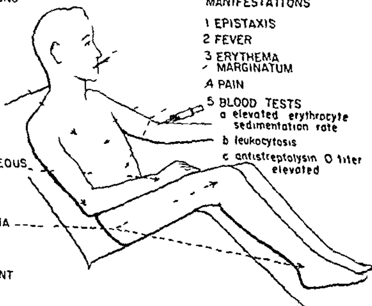


FIGURE 3 The principal signs of acute rheumatic fever are illustrated schematically According to Jones[19] a diagnosis of acute rheumatic fever is made if a patient has two *major* manifestations or one *major* and two minor manifestations These criteria are particularly valuable in gathering statistics for various types of research problems but may not be applicable to an individual patient

tissues The concept that rheumatic fever is an allergic process is based in part upon the following points (*a*) Recurrent attacks indicate an absence of immunity (*b*) The fibrinoid degeneration of collagen is considered characteristic of allergic reactions (*c*) A period of one to three weeks commonly intervenes between a streptococcal infection and the onset of rheumatic fever Such an interval is characteristic of known allergic diseases (*d*) The acute phase of rheumatic fever has clinical signs and symptoms which are frequently indistinguishable from known allergic diseases (e g , serum sickness) On this basis, individuals susceptible to rheumatic attacks may produce excessive amounts of antibody in response to repeated infections, particularly with group A hemolytic streptococci

Cavelti[15] reported that rats, injected with mixtures of killed streptococci and emulsions of rat tissues such as heart, skeletal muscle and connective tissue, developed antibodies which react in vitro with extracts of the tissue used to produce the immune reaction Some rats, immunized against mixtures of killed streptococci and myocardium or connective tissue developed valvular endocarditis with inflammatory infiltration and proliferation, particularly of the mitral and aortic valves [16] This hypothesis has not been widely accepted because the experimental observations have not been confirmed

By inducing repeated dermal infections with several types of group A streptococci, Murphy and Swift[17] were able to produce combinations of the following signs and symptoms in an inbred strain of rabbits elevated erythrocyte sedimentation rates for 1 to 2 weeks leukocytosis, anorexia weight loss, postexertional dyspnea occasional transient pulmonary rales, tachycardia, and in a few instances, definitely irregular cardiac rhythm Postmortem examination revealed granulomata with histologic characteristics strikingly similar to those of human rheumatic fever Evidence was presented that focal *infections with one type of* organism caused local and generalized hyperreactivity to other strains of the same group of organisms Since humans are prone to repeated respiratory infections with different types of group A streptococci, these experiments were designed to simulate the recurrent infectious epidoses which afflict man The implications of these studies in terms of the relationship between streptococcal infection and the reaction of the host have been reviewed by Swift [18] If the lesions produced in experimental animals by this technique actually correspond to acute rheumatic fever, accelerated progress toward an understanding of the disease and its treatment and prevention can be anticipated

The etiology of acute rheumatic fever has been considered for two reasons (*a*) the wide variety of clinical manifestations of the disease reflects the widespread distribution of lesions in different tissues and (*b*) current knowledge regarding the nature of acute rheumatic fever does not permit us to make a clear-cut distinction between this condition and myocarditis associated with other types of systemic disease

SYSTEMIC EFFECTS OF ACUTE RHEUMATIC FEVER

A definitive diagnosis of rheumatic fever can be made with confidence only when a particular patient displays a number of the systemic manifestations of the disease Until a specific test becomes universally accepted, the exact diagnosis of many patients will remain controversial Without specific criteria for the diagnosis, data on the incidence of the disease and on the effectiveness of various therapeutic attacks are difficult to evaluate For this reason Jones[19] grouped the various common signs of the disease into major and minor manifestations for the purpose of standardizing the diagnosis for statistical purposes (Fig 3) *Patients exhibiting* various combinations of these manifestations (two major *manifestations or one major* and two minor manifestations) are often regarded *as having acute rheumatic fever* These rela

oped In some patients the abdominal pain is mild and transient.

PRECORDIAL PAIN Although pain in the precordium is fairly common with acute carditis it occurs in other conditions as well including myocardial ischemia pulmonary hypertension neurocirculatory asthenia and aches or pains of nervous muscular, or skeletal origin

ERYTHEMA MARGINATUM Numerous types of skin rashes in patients with rheumatic fever have been described including urticaria erythema multiforme and petechiae However, the most significant skin lesion is erythema marginatum It usually begins on the trunk and consists of red or purplish macules which rapidly increase in area while clearing in the center to form circles or irregularly scalloped patterns These lesions appear in crops and are somewhat evanescent They are commonly seen in patients with subcutaneous nodules and have about the same clinical significance

EPISTAXIS Many patients with rheumatic fever frequently have nose bleeds without trauma The bleeding often occurs at night and is generally quite profuse and intractable The exact cause is not known

PULMONARY LESIONS *Pleurisy with or without effusion* occurs quite frequently and is often associated with pericarditis This is one cause of precordial pain but in this case the discomfort is *accentuated* by respiratory activity Diffuse inflammatory reactions in the lungs have been observed and called rheumatic pneumonitis There seems little doubt that these changes may occur but controversy persists concerning their incidence and importance

LABORATORY TESTS Leukocytosis is common in active rheumatic fever the leukocyte count being elevated from the normal range to levels above 10 000 per cubic millimeter Anemia principally microcytic is frequently encountered hemoglobin levels sometimes dropping to 7 or 8 gm per cent. The erythrocyte sedimentation rate accelerates early in the disease process and often remains increased after other signs of infection (e g white blood count body temperature) have returned to normal This test is more valuable in following the course of rheumatic attacks which have been diagnosed than as a purely diagnostic aid

The antistreptolysin titer is above normal levels following an infection with group A hemolytic streptococci The principal value of this test lies in establishing the fact that a particular patient has had contact with this group of pathogenic organisms but it may be misleading on two counts Not all strains of hemolytic streptococci produce acute rheumatic fever and, in some cases of rheumatic fever the antistreptolysin titer does not exceed normal limits Breese and Gray[20] reported that antistreptolysin titers in excess of 250 Todd units were found in 95 per cent of patients with rheumatic fever 60 per cent of cases with other streptococcal infections 4- per cent of patients with inactive rheumatic fever and 24 per cent of controls

According to Hollinger[21] attempts to differentiate between patients with active rheumatic fever and other individuals on the basis of a high antistreptolysin O titer (over 250 Todd units) would result in 10 to 30 per cent of non rheumatic conditions being misclassified as active rheumatic fever and about 25 per cent of patients with active rheumatic fever being incorrectly diagnosed However only 4 6 per cent of 197 patients with active rheumatic fever had antistreptolysin O titers of less than 50 units A single determination of the antistreptolysin titer is not nearly as informative as a series which shows the time sequence of the development and disappearance of these antibodies

The necessity for invoking a flexible and symptomologic definition of this disease (*major* and minor manifestations) indicates the wide diversity of it clinical patterns For example a patient might exhibit chorea and no other signs whatever during the first attack On a subsequent occasion, migrating polyarthritis might be the principal com-

INCIDENCE OF RECURRENT RHEUMATIC FEVER

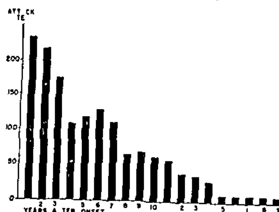


Figure 4 *The incidence of recurrent attacks of acute rheumatic fever among 1000 patients studied for 20 years by Bland and Jones* [38] *About 23 per cent of the entire group had recurrent attacks during the first year after the initial episode and thereafter the attack rate progressively diminished Although a number of patients had multiple exacerbations of the process a large proportion of the total series had recurrent attacks*

involuntary movements of the extremities may *become severe enough to interfere* with walking The condition is most likely *to occur in children, frequently without* signs of infection or any other manifestation of acute rheumatic fever Nonetheless, a majority of children with chorea ultimately suffer from rheumatic heart disease developing either insidiously or following recurrent attacks of more typical rheumatic fever

Subcutaneous Nodules Subcutaneous nodules, varying from the size of a pinhead to that of a pea or bean are most commonly found near bony prominences over the back of the elbow, the wrists the dorsum of the *hand or foot, the ankles the knees and the* skull Usually, these nodules develop in *cases with rather severe carditis and there*fore suggest a relatively grave prognosis concerning both the acute attack and the subsequent development of organic valvular disease

Previous History of Acute Rheumatic Fever Although an occasional patient succumbs to an initial attack of rheumatic fever, most patients recover without evidence of residual damage even though the episode lasts for weeks or months Murmurs and other signs of carditis usually diminish and may disappear completely However, the incidence of recurrences is so great (Fig 4) *that once a patient has suffered an attack of rheumatic fever, subsequent attacks should* be suspected whenever any of the other major or minor manifestations appear In many cases, no evidence of valvular heart disease appears following the last known attack of rheumatic fever, yet years later well developed mitral or aortic valvular lesions become apparent (see also Fig 13) The sequence *of events in the interim is com*pletely unknown, and it is frequently pre*sumed that additional attacks occurred but* were unrecognized

Minor Manifestations

The minor manifestations of rheumatic fever represent the widespread involvement of a systemic disease (Fig 3) None of them *is at all specific for this condition, they are* significant only when associated with one or *more of the major manifestations* They often serve to stimulate a search for more *definitive signs and a more prolonged ob*servation of a patient

Fever Elevated body temperature is so frequently associated with infectious processes that this sign by itself is without value Chorea may occur without fever, and acute rheumatic fever may produce a rise in body temperature no greater than that caused by a simple upper respiratory infection When fever is of unknown origin the possibility of acute rheumatic fever should be considered, *but not accepted* without definite indication

Abdominal Pain An initial attack of rheumatic fever may be indistinguishable from an attack of acute appendicitis This phenomenon is unexplained but has been attributed to inflammatory *reactions* in splanchnic blood vessels and to a number of other mechanisms Unnecessary appendectomies will continue to be performed on such patients until more specific diagnostic tests for rheumatic fever have been devel-

oped In some patients the abdominal pain is mild and transient

PRECORDIAL PAIN Although pain in the precordium is fairly common with acute carditis it occurs in other conditions as well including myocardial ischemia, pulmonary hypertension neurocirculatory asthenia, and aches or pains of nervous, muscular or skeletal origin

ERYTHEMA MARGINATUM Numerous types of skin rashes in patients with rheumatic fever have been described, including urticaria erythema multiforme and petechiae However the most significant skin lesion is erythema marginatum It usually begins on the trunk and consists of red or purplish macules which rapidly increase in a ea while clearing in the center to form circles or irregularly scalloped patterns These lesions appear in crops and are somewhat evanescent They are commonly seen in patients with subcutaneous nodules and have about the same clinical significance

EPISTAXIS Many patients with rheumatic fever frequently have nose bleeds without trauma The bleeding often occurs at ni ht and is generally quite profuse and intractable The exact cause is not known

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plaint, and a third attack might be overshadowed by abdominal symptoms simulating an acute abdominal emergency Signs of cardiac involvement might appear during any or none of these attacks On the other hand, carditis without specific extracardiac clues may appear In a disease state of such manifold complexions, any set of criteria may be misleading in an individual case For example, on the basis of Jones criteria, any patient who has experienced one attack of rheumatic fever, and who subsequently develops fever and an elevated sedimentation rate, has one major and two minor criteria and the case should be diagnosed acute rheumatic fever Obviously, rules of this type must be tempered with clinical judgment

Most of the major and minor manifestations represent changes in tissues other than the heart Although the diagnosis of acute rheumatic fever depends largely upon extracardiac signs, their severity is not a reliable index to the subsequent valvular damage Special attention should be directed toward the signs of acute carditis

Examples of Acute Rheumatic Fever

The foregoing discussion was intended to convey the impression that acute rheumatic fever is a protean disease inducing a wide variety of manifestations which can occur in any combination in either isolated or recurrent attacks With few exceptions (see Figs 2 and 6), a single bout of acute rheumatic fever is survived with little or no residual clinical or functional signs Patients developing recognizable attacks of rheumatic fever are very susceptible to recurrences, as indicated in Figure 4, and a very large proportion of these recurrent attacks are accompanied by signs of active carditis However, the signs of carditis are largely unpredictable For these reasons two specific patients are discussed to serve as bases for considering acute rheumatic carditis

The first patient, a 7 year old girl was studied during her fifth attack of acute rheumatic fever On admission to Children s Orthopedic Hospital, there was a systolic murmur, loudest at the apex, but no diastolic murmurs could be heard or recorded (Fig 5) During her stay in the hospital, she had most of the major and minor criteria of acute rheumatic fever, including a persistently elevated sedimentation rate, fever, antistreptolysin titers reaching 625 units per cubic centimeter, migrating polyarthritis in knees and ankles, and alterations in the amplitude and configuration of the P, QRS and T deflections on serial electrocardiograms (Fig 5) Seven weeks after admission (5/11/53, Figure 5), an early diastolic murmur was barely audible and a prominent early diastolic deflection was recorded sonvelographically [22] During the next month, her condition improved and the diastolic murmur disappeared The apical systolic murmur was only slightly louder than it was at the beginning of the attack Similar changes in electrocardiograms and sonvelograms have been observed in many patients with definite clinical signs of acute rheumatic fever Most of these patients survived their attacks of acute carditis and have little evidence of heart damage

Acute rheumatic carditis may be so severe that the patient succumbs to the first attack Although these overwhelming consequences of the disease are rare, an example is presented because it gives added insight into the nature of the process A robust-appearing 13 year old girl entered the Hospital with the following history Eight months before, she had noted pain and stiffness of both ankles which spread to knees and elbows There had been no antecedent respiratory infection The joint pains subsided, but returned with greater intensity and swelling 10 days later and persisted for about two weeks The sedimentation rate was elevated and the antistreptolysin O titer was 250 units per cubic centimeter, but there was no history of epistaxis rash nodules chorea or chest pain A diagnosis of acute rheumatic fever was made and therapy was instituted Her heart tones

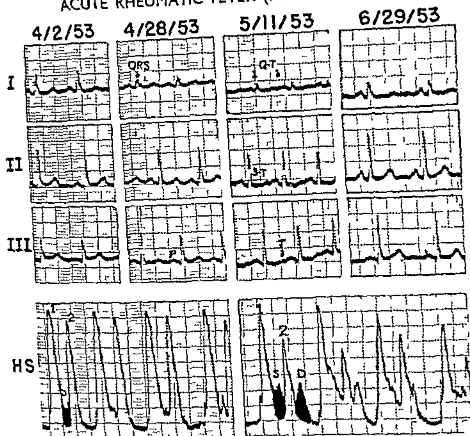


FIGURE 5 In a patient admitted during her fifth attack of acute rheumatic fever the electrocardiogram on 4/2/53 revealed slight prolongation of the QRS complex and slight elevation of S-T segment in leads II and III A systolic murmur detected by auscultation and sonelography was the only residual sign from the preceding four attacks After 26 days (4/28/53) the amplitude of QRS_1 was definitely diminished and the configuration of P waves was altered in all standard limb leads After 39 days the heart rate was faster and configurations of the P QRS and T deflections had altered from the preceding record The Q-T interval was within normal limits during the entire attack The systolic murmur had increased in intensity and an early diastolic murmur was barely audible on auscultation but clearly demonstrated sonelographically By 6/29/53 the electrocardiogram had reverted to its previous condition and the diastolic murmur had disappeared A systolic murmur persisted, only slightly louder than on admission Although this attack can be considered fairly typical wide variability in the signs and symptoms of acute rheumatic fever is its most important characteristic (Figures 5 6 12 and 13 are presented through the courtesy of the Cardiac Clinics Children s Orthopedic Hospital, Seattle Washington)

seemed distant, but a harsh systolic murmur with maximum intensity in the pulmonary area was detected and a faint diastolic rumble was heard over the apex The cardiac impulse was palpated about 1 in to the left of the mid-clavicular line She improved slowly in the hospital but the cardiac silhouette on roentgenograms enlarged progressively and four months after admission the cardiac impulse was located at the anterior axillary line During this period serial electrocardiograms disclosed alterations in T waves and S-T segments (see Fig 6) Five months after admission her condition appeared to have stabilized and she was discharged for home care with regular clinic visits During the next three months she developed progressive signs of congestive heart failure She was readmitted to the Hospital for digitalization and her condition improved greatly She returned home and appeared to be doing well on

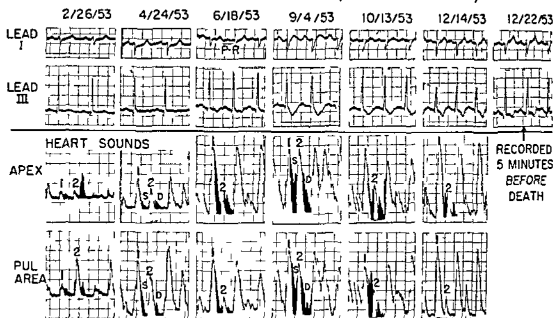


FIGURE 6 Electrocardiograms (leads I and II) and sonvelograms taken at approximately two-month intervals were selected from a large number of serial records obtained during a fatal attack of acute rheumatic fever which began eight months before the first record The amplitude and configuration of P QRS and T deflections were significantly altered Often one or more of these patterns were changed on serial records taken only a few days apart On admission the heart sounds were distant but both systolic and early diastolic murmurs were heard and recorded The sounds became progressively louder and the murmurs more intense Perhaps the most dramatic changes in the electrocardiographic patterns were the deep S waves in lead I and the marked inversion of the T waves in lead III In a record taken less than 5 minutes before the patient expired the principal change was a slight depression of S T segment in lead III Comparing these records with those in Figure 5 it is apparent that virtually any type of electrocardiographic change may occur during the course of acute rheumatic fever

12/14/53 However, one week later she was readmitted to the hospital for the last time with severe congestive heart failure Auscultation revealed a very loud first heart sound, a high-pitched 'seagull' murmur over the entire left precordium, and a rumbling diastolic murmur These murmurs were not well displayed by sonvelograms (Fig 6) One week later the patient died less than 5 minutes after an electrocardiogram was taken at the bedside The pathologic changes in the heart valves are illustrated in Figure 2 Severe pericarditis had produced fibrinous adhesions up to 0 3 cm thick, and the parietal pericardium measured up to 1 0 cm (Fig 1A) Valvulitis was prominent in the mitral, tricuspid and aortic valves The mitral valve cusps were thickened but the mitral orifice was only slightly diminished The chordae tendineae of the tricuspid valves were fused and apparently shortened but the orifice was not significantly restricted The myocardium was pale and flabby, the ventricular walls were dilated and thickened Clearly this patient developed fatal congestive heart failure because of the myocardial inflammation and not from the valvular damage Even when the clinical condition appeared greatly improved, the inflammatory process in the heart probably continued to smolder Systolic and diastolic murmurs, indistinguishable from organic mitral valvular regurgitation and stenosis, are found in patients with acute rheumatic fever and having only slight or moderate valvular deformity as did the patient under consideration

THE ORIGIN OF SIGNS FROM ACUTE CARDITIS

Causes of Auscultatory Signs of Acute Rheumatic Carditis

Although the changes in heart sounds and murmurs are by no means uniform, common

auscultatory observations include (*a*) nonspecific changes in the first heart sound (*b*) early systolic murmurs (*c*) intensified third heart sound or protodiastolic gallop, (*d*) early or mid-diastolic rumble and (*e*) presystolic crescendo sounds or murmurs The murmurs which develop during acute rheumatic fever often closely resemble those typically associated with mitral stenosis (see Chapter 18) For example the murmurs illustrated in Figure 6 simulated those of advanced mitral stenosis even though the mitral orifice was not significantly restricted (Fig 2) Furthermore such murmurs appear during acute attacks of rheumatic fever and regress or disappear as the patient recovers (Fig 5) Although many theories concerning the various auscultatory signs of acute carditis have been offered none has been universally accepted Old and new concepts will be discussed in relation to recent experiments in which attempts were made to produce heart murmurs by inducing changes in the function of the mitral valves

Systolic Murmurs Patients with rheumatic carditis characteristically have apical systolic murmurs of at least moderate intensity [23 24] These systolic murmurs usually appear early in the attack of myocarditis and persist long after the attack is ended often indefinitely There has been a widespread tendency to ascribe such murmurs to regurgitation of blood through the mitral valve into the left atrium (mitral insufficiency) At least three mechanisms could account for incomplete closure of the mitral valves (*a*) the area of the valve cusps is too small (*b*) the mitral orifice is enlarged or (*c*) the cusps cannot meet and seal However the murmur may not be due to changes in the valve at all The area of the valve cusps is much larger than the normal mitral orifice and the mitral valve must be very severely retracted or deformed *before* significant mitral regurgitation occurs Thus mitral incompetence *from* reduced valve area occurs only at a very advanced stage of mitral valvular disease requires years to develop and cannot be responsible for the transient murmurs developing during attacks of acute rheumatic fever

The mitral valve ring theoretically could dilate until the area of the valve cusps was insufficient to close the orifice However, the area of the normal cusps greatly exceeds the area of the orifice so a rather extreme dilatation of the ring would presumably be required Furthermore the mitral ring is a fibrous structure and a transient and reversible dilatation of the ring would involve proliferation and resorption of dense connective tissue Dilatation of the valve ring also implies extensive dilatation of the ventricles which is not consistently detected roentgenographically during attacks of acute rheumatic fever Mitral regurgitation could result if something prevented complete apposition of the valve cusps For example thickening of the valve edges and formation of verrucae could theoretically produce slight valve separation through which blood could *regurgitate at high* velocity into the atrium producing turbulence and systolic vibrations Although this explanation has been suggested by many authors and seems applicable it was not confirmed by experimental observations on *dogs*

Heart sounds were recorded before and after inducing various types of lesions and restraints on the mitral valves of dogs Verrucous lesions and nodules formed along *the line* of mitral valve closure after Lipiodol was injected at numerous points around the mitral valve ring (Fig 7) or when multiple silver clips were applied to the valve edges While systolic murmurs were generally *recorded after the* operation these were *usually* no more obvious than the systolic murmurs consistently noted on the control records (*Fig 7*) Silver chains were also fastened in different locations *to* and through the mitral valve cusps The delicate chains were very flexible when installed *within the heart* but soon became thickened and stiffened by thick layers of fibrin (Fig 8) *The* chains presumably did not produce

EXPERIMENTAL MITRAL LESIONS

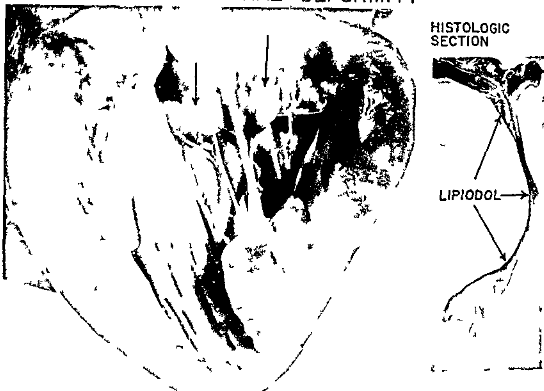




FIGURE 7 During preliminary experiments directed toward opacifying heart valves so that their movements might be recorded cinefluorographically Lipiodol was injected into the region of the mitral valve ring at several points around its circumference In several animals verrucous lesions developed along the valve edges

A Gross deformities of the mitral valve cusps were discovered several weeks after Lipiodol injections which effectively opacified portions of the valve cusps The nodular swelling and irregularity of the valve were not due solely to accumulation of Lipiodol which actually was found on histologic section to be confined to a very thin layer just under the ventricular surface of the valve cusps The cause of this extreme thickening and deformity is not clear and was not produced to this extent on subsequent trials

B Small verrucous nodules along the line of valve closure were observed after Lipiodol injection in several animals These lesions resemble those observed in patients with acute rheumatic fever (see Fig 2*B*) but were not associated with significant systolic or diastolic murmurs as judged by both auscultation and phonocardiograms

significant turbulence by themselves since no diastolic vibrations were recorded when a chain was stretched across the atrium just above the mitral orifice In fact the systolic murmur noted in the preoperative control record was virtually absent on records taken 34 days after the operation In its place a sharp systolic spike appeared simulating heart sound records of a systolic click (Fig 8 A) Chains passing through the



FIGURE 8 Changes in heart sounds produced by fibrin-covered chains in various positions within the heart were selected from a series of experiments on the movements of the mitral valve in the intact unanesthetized dog

A In the preoperative control record an early systolic murmur was present (SM) Such murmurs are frequently recorded in normal dogs A silver chain was installed directly over the mitral orifice and 34 days later phonocardiographic records revealed neither a systolic nor a diastolic murmur but a sharp spike appeared in early systole This sharp deflection simulates the records obtained in the presence of an audible systolic click

B Two chains passing through the mitral orifice were attached to the atrial and ventricular walls at either end After 29 days the chains were adherent to *chordae tendineae*, but not to the valve cusps A definite systolic murmur was recorded from the region of the apical impulse but it was not definitely more pronounced than that recorded before the surgery was performed

C A doubled chain fastened to the atrial wall and to the edge of the anteromedial mitral cusp clearly restricted movement of the valve cusp and an abnormally loud systolic murmur was recorded No diastolic murmur was noted on phonocardiograms by auscultation, or by amplifying the sounds recorded on tape

D A chain attached to the mitral valve ring at one end passed through the mitral valve to the ventricular wall on the opposite side The chain became firmly adherent to the valve cusp and was covered with a heavy accumulation of fibrin A prominent systolic murmur was heard and confirmed on heart sound records A presystolic murmur was noted by auscultation, but could not be definitely established phonocardiographically This was the only suggestion of a *diastolic* murmur noted in the entire series

mitral valves and fastened to the ventricular wall by elastic bands became adherent to the valve cusps They could interfere with valve closure in the same way as nodules, but actually made little difference in the systolic murmurs (Fig 8*B*) Significant murmurs were produced in only two dogs in the entire series (Fig 8*C*, *D*) Thus, these experiments failed to indicate any exact mechanism for the production of systolic murmurs by valvular deformity They gave little support to the concept that interference with valve closure by verrucae or minor valve deformities is an important mechanism

The systolic murmurs in acute carditis usually appear in early systole They have relatively high frequency and a "blowing" quality Unfortunately, systolic murmurs with these characteristics are frequently noted in individuals with entirely normal hearts[25] This brings up the possibility that the systolic murmurs heard during acute carditis are *not necessarily a result of mitral* regurgitation For example, the aortic leaf of the mitral valve acts as a baffle which deflects blood toward the aortic orifice Rapid blood flow past irregularities on the mitral leaflets might produce eddy currents and turbulence with sufficient intensity to produce audible systolic murmurs The flow velocities in the root of the aorta are normally sufficient to produce turbulence as evidenced by functional murmurs (see Fig 16, Chapter 13) Clearly, the mechanisms underlying the production of systolic murmurs during acute carditis have not yet been elucidated

INTENSIFIED THIRD HEART SOUND A gallop rhythm, developing during acute myocarditis, generally signifies an increased intensity of the third heart sound The third heart sound is heard in a fairly large proportion of children and corresponding vibrations can be recorded on phonocardiograms from virtually all individuals even when they are inaudible[26] Third heart sounds gain intensity presumably from either increased rate of early diastolic filling[27] or a change in the elastic properties of the ventricles In other words the velocity attained during rapid filling must be greater or the transition between rapid filling and slow filling must be more abrupt Since early diastolic murmurs are also prone to develop during myocarditis, a more rapid filling in early diastole might explain both phenomena This would imply either a steeper atrioventricular pressure gradient or an increased ventricular distensibility Clearly, some of these mechanisms must be involved in the production of the observed gallop rhythm, but at present, no explanation is based on direct experimental evidence

DIASTOLIC MURMURS The most puzzling feature of the murmurs accompanying acute myocarditis is their very close resemblance to the murmurs of advanced organic mitral stenosis Murmurs appear primarily during two phases of diastole A low-frequency, rumbling sound characteristically *occurs in early and mid-diastole* In late diastole, a rough crescendo (presystolic) murmur seems to gain intensity rapidly and terminate in a *loud first sound Such diastolic* murmurs often cannot be distinguished from those of advanced mitral stenosis and yet they usually disappear *completely as the* rheumatic fever subsides The origin of turbulence during diastolic filling seems fairly obvious when the mitral orifice becomes seriously restricted by scarring and fusion of the valve cusps (Fig 18A, Chapter 13) However, the basic causes of early diastolic and presystolic murmurs during acute carditis are not easily explained because the mitral orifice is usually not obstructed (see Fig 2) Since the murmurs appearing in early diastole and in late diastole present somewhat different problems they will be considered individually

Taquini et al[23] found that the early diastolic murmurs began at the transition from rapid filling to the slow filling phase and suggested that the diastolic rumble could be an acoustic effect produced by an intensified third heart sound in some patients In others the third and fourth heart

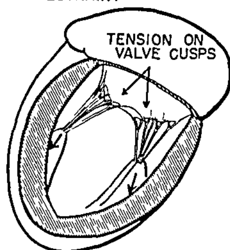
sounds might be brought into close temporal sequence by tachycardia enhancing the acoustic effect of a rumble In other words these authors class the early diastolic murmurs as auditory illusions resulting from intensification of vibrations which occur normally Since auditory perception is extremely insensitive to low-frequency vibrations diastolic sounds might reach threshold during an attack of carditis and disappear during recovery just as the murmurs may disappear in certain patients with definite organic mitral stenosis [28, 29] Such an explanation is superficially satisfying but does not completely account for the occurrence of such auditory illusions in patients with acute carditis and not in normal patients of the same age These early diastolic vibrations persist long after a normal third heart sound (Figs 5 and 6) The rapid flow of blood past thickened irregular valve cusps is a suggested cause of turbulence and diastolic vibrations However early diastolic murmurs were not definitely elicited in any of the experimental animals with vegetations and foreign bodies on and between the valve cusps (Figs 7 and 8) The filling of the ventricles might occur more rapidly producing intensification of the third heart sound and greater turbulence However the murmurs usually begin after the most rapid filling phase is completed so more rapid filling between the second and third heart sounds would not easily account for vibrations extending far into the slow filling phase

In patients with acute myocarditis one often hears presystolic murmurs which also closely resemble similar murmurs of mitral stenosis These murmurs have also been classed as auditory illusions by Alimurung et al [30] They concluded that the impression of a presystolic murmur might result from one of several factors (*a*) prolongation of the first sound with intensification of later elements (*b*) splitting of the first sound with the second element more intense than the first and (*c*) audible vibrations of atrial origin preceding the first sound These factors were demonstrated on stethograms obtained from patients with presystolic murmurs reported after auscultation but they can also be found on stethograms from subjects in which auscultation gives no suggestion of presystolic murmurs

Bland White and Jones[31] demonstrated that apical diastolic murmurs occur in patients in whom the mitral valve circumference is normal or larger than normal Since similar murmurs were perceived in some patients with minimal valve deformity and in others with definite mitral stenosis, these authors postulated that relative mitral stenosis might be produced by ventricular dilatation In other words if the ventricle dilated and the fibrous mitral ring retained the same dimension, the mitral orifice would be smaller in relation to the size of the ventricular cavity (Fig 9*B*) It is generally recognized that acute myocarditis produces some enlargement of the cardiac chambers In fact, the actual increase in volume may be considerably greater than the apparent change on roentgenograms as a 50 per cent increase in heart volume may cause only a 14 per cent increase in any one of its dimensions [3] However, sufficient difference in dimensions between the mitral ring and the ventricular chamber to produce turbulence (see Fig 15 Chapter 13) would appear to require extreme ventricular dilatation The concept of a 'functional mitral stenosis suggested by White Bland and Jones leads to consideration of a possible mechanism which to my knowledge has not been suggested previously

FUNCTIONAL MITRAL STENOSIS Cinefluorographic studies disclosed that the movements of the mitral valve cusps in experimental animals were quite limited (Fig 8 Chapter 13) This observation suggested that the mobility of the mitral cusps may be restricted by traction exerted through the chordae tendineae During diastole ventricular filling distends the chamber increasing the distance from the end of the papillary muscles to the mitral ring Fibrous structures such as the chordae

FUNCTIONAL MITRAL STENOSIS



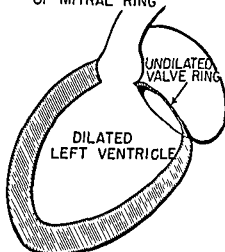


FIGURE 9 The etiology of systolic and diastolic murmurs in acute rheumatic carditis has never been established Two possible mechanisms are illustrated schematically but are unsupported by any direct experimental evidence

A If tension is exerted on the mitral valves through the chordae tendineae by normal maximal diastolic filling or by contraction of papillary muscles during systole dilatation of the ventricle would increase this tension because the papillary muscles would be farther separated from the valve rings If the movements of mitral valve cusps are abnormally restricted by this tension the valve could be prevented from either opening fully or closing completely this situation could produce diastolic and systolic murmurs

B Bland White and Jones[27] suggested that dilatation of the left ventricle without corresponding expansion of the fibrous mitral valve ring could produce a relative mitral stenosis which might lead to diastolic murmurs

tendineae and the valve cusps do not participate in this lengthening and may be put under some tension Atrial contraction suddenly adds an additional increment of blood to the ventricular chambers which would presumably add slightly to the tension on the valve cusps and possibly draw them toward apposition During ventricular systole, the papillary muscles and the ventricular wall contract together and the tension on the valves is greatly increased by the high interventricular pressure However, the valves are apparently not displaced very far by this high pressure, indicating that the pressure is being countered by increased tension exerted through the papillary muscles During relaxation of the ventricular walls, the papillary muscles also lengthen Under these circumstances, it is possible that tension on the chordae tendineae can persist throughout much of the cardiac cycle owing to the contraction and relaxation of the papillary muscles If myocarditis produces acute ventricular dilatation, the tension exerted on the valve cusps might increase Since the chordae tendineae from both cusps of the mitral valve arise from the same or adjacent papillary muscles, this increased tension should draw the valve cusps together For example, imagine two pieces of canvas fastened around the circumference of a metal hoop with guy ropes fastened in the same relative positions as the chordae tendineae Two men on opposite sides of the hoop pulling in opposite directions on the two sets of guy ropes would tend to approximate the pieces of canvas like a flutter valve Abrupt dilatation of the ventricular chambers could theoretically have a similar effect, a functional stenosis of the valve being produced by the restraining force which the papillary muscles exert on the valve cusps This splinting of mitral valve movement would persist as long as the increased tension remained It would be relieved by the recovery of the myocardium

if the ventricle resumed its normal dimensions A persistent dilatation could be countered by lengthening of the papillary muscles or proliferation of valves and chordae tendineae If functional mitral stenosis were responsible for diastolic vibrations it should operate whenever the ventricles become dilated For example this mechanism could apply to the Austin Flint murmur associated with massive ventricular dilatation from aortic insufficiency Patients with hyperthyroidism sometimes develop apical murmurs simulating mitral stenosis (see Chapter 16) Occasionally patients with dilated hearts from various causes may exhibit perplexing diastolic murmurs This hypothesis lacks direct experimental evidence and is presented merely to indicate that transient diastolic murmurs might be produced by functional changes in the heart rather than by acoustic illusions

Roentgenographic Signs of Rheumatic Carditis

Many clinicians assert that congestive failure in the absence of active myocarditis is rare in young persons This attitude is probably justified in most cases excluding certain types of cardiovascular disease such as serious congenital malformations of the heart or pulmonary hypertension of various types Enlargement of the heart with signs of congestive heart failure frequently accompanies severe attacks of carditis A patient with fatal acute rheumatic fever usually has massive cardiac enlargement during the greater part of the episode (Figs 2 6) Dilatation of the heart during myocarditis is usually generalized so the configuration of the cardiac silhouette is not altered in any characteristic fashion Slight degrees of cardiac enlargement are difficult to detect for reasons which have been presented in Chapter 11 A progressive increase in heart size demonstrated by serial roentgenographic examinations is more significant and more readily distinguished than a similar degree of apparent cardiac enlargement observed on the initial examination According to Keith and Brick [33] the heart size may increase moderately within the first two or three weeks but enlargement appears to occur slowly at any stage of the disease Acute dilatation with a dramatic change in heart size is rare

Electrocardiographic Signs of Acute Rheumatic Carditis

Reflecting the widely diversified character of rheumatic myocarditis, changes in electrocardiographic complexes follow no characteristic pattern during the disease In some patients the electrocardiograms may not change significantly In any particular case, any or all aspects of cardiac electrical activity may be modified Disturbed conduction through the atria atrioventricular node and ventricles may alter the P wave P-R interval QRS complex and cause secondary alterations in the S-T T complex (see Chapter 15) Prolongation of the P-R interval is an expression of retarded atrioventricular conduction and can be more easily detected and evaluated than any other alteration in the complexes If the established criteria for the upper limits of normal P R interval are used first degree atrioventricular block appears at some time during the course of acute rheumatic carditis in about 80 per cent of patients However the P R interval tends to vary widely and may exceed normal limits only on a single day so serial electrocardiograms must be taken at frequent intervals to demonstrate significant changes in many individuals

In the author s opinion, prolongation of the P-R interval has been too definitely identified with acute rheumatic carditis and has been overemphasized partly because the criteria for abnormality are well established

CHANGES IN P WAVES Alterations in the P waves may take many forms including depression or inversion notching or diphasic form widening or increased amplitude (see Fig 10D) The exact type of configuration assumed is not nearly as important as the

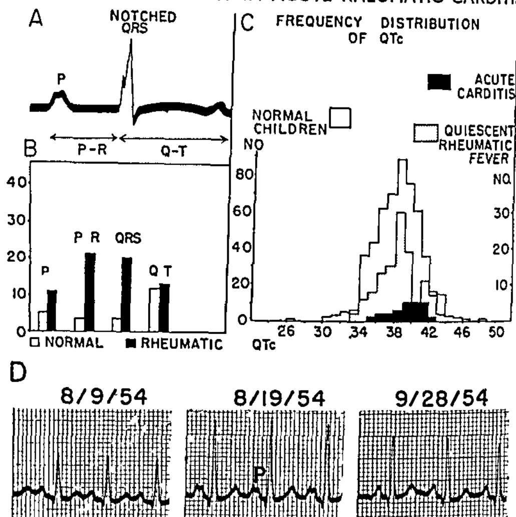


FIGURE 10 *A* Alterations in electrocardiographic complexes during acute rheumatic carditis are illustrated schematically Changes in the amplitude and configuration of P waves are frequently observed Prolongation of the P R interval beyond limits of normal is a widely recognized sign Altered amplitude and configuration of QRS are characteristically observed and a common form is the appearance of notching Many clinicians emphasize prolongation of the Q-T interval

B The incidence of certain electrocardiographic signs in 46 young patients with acute rheumatic fever and in 46 normal children was determined by Price [34] In 5 normal subjects and 11 patients the amplitude and duration of P waves was outside established arbitrary limits Prolongation of the P R interval and notching of the QRS complex occurred with about equal frequency but often in different individuals The duration of the Q-T interval exceeded arbitrary limits in about the same number of normal children and patients with acute rheumatic fever

C The frequency distribution for QT_c among a large group of subjects was determined by Alimurung et al [36] The average value for QT_c among 517 infants and children was 0 404 with a standard deviation of 0 026 The values ranged from about 0 28 to 0 50 The distributions of QT_c in 143 patients with acute rheumatic fever and in patients with quiescent rheumatic heart disease fall near the center of this range The overlap of values for QT_c in normal individuals and in patients with acute rheumatic carditis provides graphic evidence that this measurement is not particularly useful as a diagnostic sign (From Craige E Alimurung M M Bland E F and Massell B F [37])

D A prolonged flattened notched P wave appeared and regressed in a patient with acute rheumatic fever The type of P wave which appeared on 8/9/54 closely resembles the P mitrale which characteristically persists for many years in patients with mitral stenosis (See Fig 23*B* Chapter 15)

fact that a significant change occurs within relatively brief intervals on serial electrocardiograms

CHANGES IN QRS COMPLEX If one examines a large series of electrocardiograms obtained from unselected school children the predominance of sharp clean QRS complexes of brief duration is very striking In

contrast, electrocardiograms obtained from patients with histories of acute rheumatic fever often display more prolonged QRS complexes with a fairly high incidence of slurring or notching of the individual deflections (Fig 4 Chapter 15) Cardiologists dealing principally with adults tend to class slurring and notching of QRS complexes among the normal variants In the early sta es of acute rheumatic carditis, QRS complexes of low amplitude (less than 0 5 mV) are frequently observed in lead I without evidence of pericardial effusion These low-potential deflections persist for varying periods but in many cases the QRS interval may increase on serial electrocardiograms or the amplitude of the waves may become progressively higher as slurring and notching develop on the various components of the complex. Price[34] found that the incidence of notched QRS complexes in acute rheumatic fever and in recurrent attacks was almost as great as that of prolongation of the P R interval *Notching of complexes* persisted longer than first degree atrioventricular block so it was the most common electrocardiographic abnormality seen during the quiescent pha e following previous rheumatic episodes More severe degrees of ventricular conduction disturbance such as bundle branch block are relatively rare

CHANGES IN S-T AND T COMPLEX. Perhaps the most common electrocardiographic alteration during acute myocarditis is a change in the amplitude and configuration of T waves Since the form of the T wave is somewhat labile even in normal individuals variations should be interpreted with caution In serial electrocardiograms the T waves may become elevated depressed notched diphasic or inverted during the course of acute myocarditis Deviation of the S-T segment is uncommon but has greater significance than changes *in the form* of the T waves In general the S-T segment tends to be displaced in the same direction as the T wave presumably due to inflammatory processes in the subepicardial region. In some patients changes in S-T and T complex may simulate those of myocardial ischemia or infarction

THE Q-T INTERVAL. The total duration of electrical activity in the ventricles during systole is indicated by the interval between the beginning of the QRS complex and the end of the T wave (Q-T interval) Some clinicians consider prolongation of this interval an important sign in acute rheumatic fever Because it is greatly influenced by tachycardia the Q-T interval is frequently corrected for heart rate This corrected value (QT_c) may be divided by the ideal Q-T interval for the particular patient, producing the Q-T ratio If the Q-T ratio exceeds an arbitrary value (1 08 for men and children) the Q-T interval is considered prolonged This process can be facilitated by using appropriate nomograms, but will not be discussed further because the measurement has doubtful value in the recognition of acute rheumatic fever For example Pokress and Goldberger[35] found prolongation of the Q-T ratio beyond the maximal normal value in only 28 of 100 patients with acute rheumatic fever The *variability in the Q-T* interval among 517 normal infants and children[36] was compared to that in the Q-T interval in 143 rheumatic children between the ages of 7 and 14 years[37] Twenty nine patients with fatal pancarditis had Q-T intervals within the normal range Changes in the Q-T interval paralleled changes in the clinical conditions in two-thirds to three-quarters of the cases, but obvious discrepancies were also noted The frequency distribution curve of Q-T intervals in patients with rheumatic fever *was confined* within that for normal children (Fig 10) This observation is consistent with my own experience that the Q-T interval has little value in the detection of acute rheumatic fever

EVALUATION OF ELECTROCARDIOGRAPHIC CHANGES The diverse electrocardiographic patterns which occur during acute rheumatic myocarditis signify that a single electrocardiographic tracing has relatively little value On the other hand careful com-

parison of serial electrocardiograms will bring to light progressive changes in patterns in virtually all patients with acute rheumatic fever plus a large number of patients with a wide variety of other febrile illnesses If one assumes that significant changes in electrocardiographic patterns indicate changing functional conditions in the myocardium, this test becomes exceedingly sensitive

SEQUELAE OF RECURRENT RHEUMATIC FEVER

If rheumatic fever and carditis were self limited so that no further functional or organic damage followed a single attack it would be a relatively small clinical problem Most patients would recover completely with little residual sign except for soft apical systolic murmurs, some of which disappear in time The principal therapeutic problem would center around supportive therapy to facilitate survival of the immediate attack Unfortunately, this state of affairs bears little resemblance to the problem presented by rheumatic fever For example, Bland and Jones[38] reported a follow-up study for 20 years on 1000 patients with rheumatic fever in childhood The average age at onset for this group was eight years From these data, the status of the group on discharge from the hospital, and after 10 and 20 years, has been plotted in Figure 11 Of 87 patients with systolic murmur at the apex, the mur

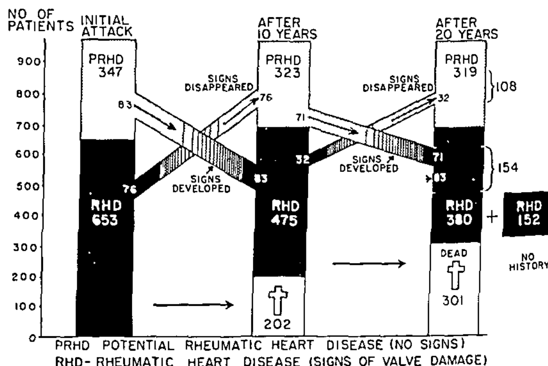


FIGURE 11 A series of 1000 consecutive patients with rheumatic fever chorea or rheumatic heart disease has been followed for 20 years The original status of these patients on discharge from the hospital is indicated under the heading Initial Attack No clinical evidence of rheumatic heart disease was found in 347 patients who were therefore classified as potential rheumatic heart disease The remaining 653 had evidence of rheumatic heart disease such as significant murmurs

During the next 10 years clinical evidence of rheumatic heart disease developed in 83 patients previously classified as potential rheumatic heart disease while signs of heart disease disappeared in 76 patients Two hundred and two patients died

At the end of 20 years 71 more patients developed signs of rheumatic heart disease making a total of 154 in whom evidence of heart disease developed at varying intervals after the initial attack Among adult patients with rheumatic heart disease about 40 per cent have no history of any attack of acute rheumatic fever It is interesting that in this study about the same percentage developed signs of rheumatic heart disease at varying intervals after a definite rheumatic episode In 32 additional patients the signs of rheumatic heart disease disappeared and 99 more patients died (total 301) (From data presented by Bland E F and Jones T D[38])

mur disappeared in about one-third and remained unchanged in another third. Another group of about the same size developed a diastolic murmur indicative of mitral stenosis.

The ultimate effects of an attack of rheumatic fever are not established for many years (Fig. 11). In a large proportion of patients signs of valvular damage disappear while other patients acquire signs of organic valvular deformity with or without obvious recurrence of acute rheumatic fever. The tardy development of serious valvular disease suggests a very pertinent question. Does active myocarditis and valvulitis smolder undetected for many years after acute rheumatic fever? Recent evidence indicates that this can occur. During surgical correction of mitral valve deformities the left atrial appendage is routinely excised and about 50 per cent of these appendages contain Aschoff nodules.[39-43] Such acute inflammatory lesions appearing in the atrial appendage are generally accompanied by similar lesions in the remainder of the heart, particularly the left ventricle. Furthermore there is evidence that rheumatic fever may be reactivated by mitral surgery in patients with no preoperative evidence of carditis.[44] These observations are extremely disturbing because cardiac surgery is not elected in the presence of any evidence of active carditis. Thus a very large group of older patients with no history of active rheumatic fever for many years are found to have histologic evidence of rheumatic activity within the heart muscle. Either the Aschoff nodule and the criteria for active rheumatic carditis are not as specific as previously believed or these patients had subclinical rheumatic activity for many years. If active myocarditis and valvulitis can simmer undetected for 30 or 40 years, how long should prophylaxis continue? Will prevention of streptococcal infections by prophylactic administration of antibiotics eliminate external signs of rheumatic fever without suppressing the progressive development of valvular disease? It is too early to assess the implications of these questions.

In the meantime entirely new concepts concerning the nature and development of acquired valvular disease are evolving from the rapidly expanding experience with cardiac surgery and cardiac catheterization. Direct knowledge of cardiac function and disease derived from living patients is exposing the inadequacy of previous physiologic, clinical and pathologic interpretations. This applies particularly to rheumatic mitral valvular disease, which will be considered in some detail in the next chapter.

ACUTE NON-SPECIFIC MYOCARDITIS

Changes in electrocardiographic patterns similar to those observed in the course of acute rheumatic fever are observed in a wide variety of clinical conditions. Diphtheria has long been recognized as a cause of serious cardiac complications. In recent years significant changes in serial electrocardiograms have been reported in the course of many other infectious diseases.[45-47] Pathologic signs of myocardial inflammation have also been discovered in a broad spectrum of disease states.[2-4] Occasionally, myocarditis develops in the course of subacute bacterial endocarditis,[48] but in the majority of instances organisms in the myocardium are not demonstrable. Lepeschkin[46] presented an extensive bibliography concerning the etiology of myocarditis and some representative examples are listed in Table 10. A

TABLE 10. CLINICAL CONDITIONS WHICH MAY PRODUCE ELECTROCARDIOGRAPHIC EVIDENCE OF MYOCARDITIS

Acute rheumatic fever	Brucellosis
Streptococcal respiratory infections	Syphilis
Diphtheria	Malaria
Scarlet fever	Glomerulonephritis
Otitis media	Measles
Pneumonia	Parotitis
Cholecystitis	Epidemic hepatitis
Appendicitis	Poliomyelitis
Erysipelas	Typhus
Gastro-enteritis	Scrub typhus
Typhoid fever	Anaphylactic shock
Meningitis	Urticaria

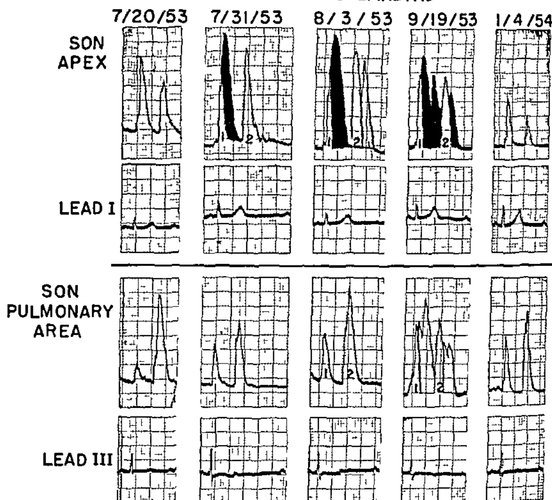


FIGURE 12 Serial electrocardiograms and sonvelograms are presented from a patient who did not demonstrate the classic manifestations of acute rheumatic fever Minor changes in QRS and T deflections are apparent particularly in lead III (S-T T and initial deflection of QRS) After 7/31/53 the patient had no symptoms or signs Yet on 9/19/53 definite systolic murmurs and early diastolic murmurs were heard and prominently displayed on sonvelograms They disappeared completely by 1/4/54

discussion of the various ramifications of this extensive list is not considered appropriate The kind of clinical problem which may be encountered is illustrated by two case reports [22]

Alterations in electrocardiographic patterns and heart sounds with the development of murmurs may suggest acute myocarditis when other clinical signs are equivocal An 8 year old boy was treated for abscessed teeth for one week prior to admission to Children's Orthopedic Hospital During this period he had an elevated leukocyte count (21,000 cells), elevated erythrocyte sedimentation rate and fever up to 103 F One day before admission his right wrist and both knees were slightly tender but the discomfort disappeared by the next day and did not recur He complained of transient pain in the chest and abdomen for a few hours The antistreptolysin O titer was 166 units The fever diminished after five days of antibiotic therapy and the abscessed teeth were extracted The sedimentation rate gradually declined and the patient became completely asymptomatic A routine electrocardiogram was within normal limits but was sufficiently suspicious to call for a second record Despite normal laboratory tests and the complete absence of clinical signs serial electrocardiograms and sonvelograms displayed alterations in patterns of the types ordinarily observed in patients with acute carditis (Fig 12) If these signs

ard symptoms had developed in a patient with previous attacks of acute rheumatic fever such an episode would probably have been labeled a recurrence of this disease

Another example of this problem was the case of a girl 5½ years of age, who was seen after a febrile illness of 15 days beginning abruptly with a severe headache repeated vomiting and fever (103 to 104° F) Extensive tests in another hospital were negative but antibiotics were administered Fever (99 to 100° F) persisted for 12 days Body temperature rose again to 103° F on the day of admission at which time the leukocytes numbered 9550 the erythrocyte sedimentation rate was 14 mm and the antistreptolysin titer was 12 units per cubic centimeter of serum Electrocardiograms revealed a P-R interval of 0 18 (upper limits for this age and heart rate, 0 165) and QRS_1 of low potential (2 mm) Auscultation of the heart revealed nothing remarkable although the sonvelogram exhibited a very low intensity first heart sound with an early systolic murmur (4/14/53 Fig 13) Three weeks later (5/4/53) electrocardiograms revealed that the R wave in lead I had an increased amplitude and slight slurring the P R interval had

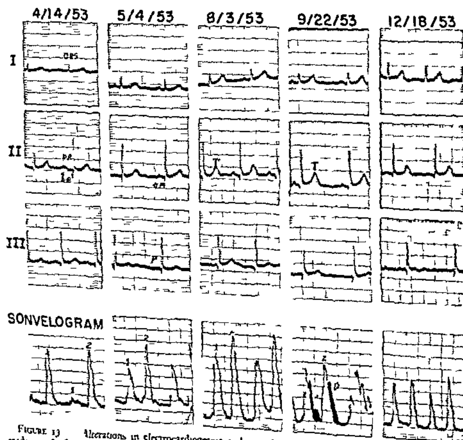


FIGURE 13 Alterations in electrocardiograms and sonvelograms occurred in a patient with minimal evidence of infectious disease A small QRS_1 is a common occurrence in patients with definite acute rheumatic fever The P R interval (0 18) was beyond the upper limits of normal on 4/14 53 The P wave in lead III be came isoelectric on 5/4 53 T wa es in lead II became taller until 9/22/53 and then diminished. T waves in lead III became inverted on 12/18/53 The first heart sound was muffled on 4/14/53 but became progressively louder as a systol c murmur was heard and recorded on 9/22/53 A prominent early diastolic deflection was noted on the son elograms taken on 9/22/53 but an early diastol c murmur was not definitely established dur ing auscultation. There is no way of knowing whether this patient had atypical acute rheumatic fever acute non-specific myocarditis or non-specific changes of unknown etiology

diminished to 0 14 and P_{III} had become isoelectric The first sound at the apex and the systolic murmur had become more prominent on the sonvelogram Three months later (8/3/53), QRS_I had become more prolonged, T_{II} had greater amplitude with slight elevation of the S-T segment, and P_{III} had reappeared During this entire period, the patient had been afebrile and asymptomatic, with normal laboratory tests On September 22, 1953, T_{II} had become higher, P_{III} had disappeared, and prominent systolic and early diastolic sounds were recorded on the sonvelograph

This patient had no evidence of streptococcal infection at any time during the entire episode The chief complaints were gastro-intestinal disturbances (vomiting and mild diarrhea) The electrocardiographic and sonvelographic records are consistent with a diagnosis of carditis (a major manifestation of rheumatic fever), and prolonged fever is a minor manifestation of rheumatic fever However, acute rheumatic fever cannot be diagnosed with any confidence on the available evidence During the past year, 16 similar diagnostic problems have been encountered The proper diagnosis and treatment of such patients remains controversial A great many questions of practical importance arise in cases of this sort Should this episode be classed as a non-specific myocarditis from which no future cardiac complications can be expected? Are these children among the 40 per cent of patients who develop "rheumatic' valvular heart disease without any definite signs of acute rheumatic fever Should special attention be directed toward protecting this patient from streptococcal infections? Do these recorded cardiac changes justify initiation of a protracted prophylactic regime of antibiotic therapy?

The answers to these questions remain highly controversial because any one of the several attitudes could be easily justified These patients were selected to represent a large number of problems which will continue to arise until more specific diagnostic tests for acute rheumatic fever have been developed, and until it is certain that carditis of non-specific origin does not produce valvular deformities At the present time careful studies extended for long periods are the only reasonable approach to such problems The therapeutic attack will have to be based on sound clinical judgment in the individual case

If all acquired valvular disease is universally attributed to previous acute rheumatic fever even in those cases in which this relationship cannot be established, this criterion automatically precludes establishing non-specific myocarditis as a possible etiologic factor in valvular damage So long as no acute phase of carditis is detected in some 40 per cent of patients with acquired valvular damage, we cannot afford to exclude the possibility that non-specific myocarditis can play a role in at least some of these patients

SUMMARY

Inflammatory lesions of the heart and valves are the most important cause of acquired heart disease in childhood Acute inflammatory processes in the myocardium occur in a large percentage of patients with acute rheumatic fever, which is a systemic disease affecting connective tissues in many parts of the body A single attack of acute rheumatic carditis is usually survived and often leaves no residual damage of functional significance Recurrent episodes of acute rheumatic fever or smoldering inflammatory lesions in the region of the valves frequently lead to scarring and deformity of the heart valves (most commonly the mitral valve)

The early diagnosis of acute rheumatic fever has assumed far greater practical importance since the advent of prophylactic antibiotic therapy, which markedly reduces the incidence of recurrent attacks However, the manifestations of this disease are so non-specific and variable that definitive diagnosis is often most difficult Lacking a specific test for acute rheumatic fever, the disease is usually recognized by systemic

manifestations rather than by changes referable to the heart A wide variety of disease states produces clinical signs closely resembling those associated with acute rheumatic fever Such acute non-specific myocarditis is not generally believed to produce chronic valvular lesions About 40 per cent of patients with evidence of valvular disease are adults with no history of any previous attack of acute rheumatic fever Until the causative factors in this large proportion of patients can be established it seems unwise to ignore the possibility that at least some of these were originally among the very large number of patients who develop non specific carditis at some time during their life span A specific test for acute rheumatic carditis is sorely needed to help solve both the theoretical and practical problems presented by this perplexing disease entity In the meantime each patient must be carefully considered individually in establishing both the diagnosis and the appropriate therapy An incorrect diagnosis of acute rheumatic fever followed by prophylactic treatment with prolonged courses of anti biotic therapy involves both the expenditure of time and money and the possibility of producing a cardiac invalid from an essentially normal person Alternately failure to prevent recurrent attacks of rheumatic fever by adequate prophylaxis may lead to progressive valvular deformity and serious heart disease Treading the narrow line between these dangerous alternatives requires balanced judgment

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Chapter 18

Valvular Disease

The ventricles can function as efficient pumps only if the inflow and outflow valves open adequately and close effectively. Deformities of the valves produce two main types of functional disturbance: stenosis and regurgitation. Valvular stenosis produces increased resistance to flow through restricted valvular orifices. Valvular incompetence or insufficiency implies that the valves fail to close and seal, allowing blood to regurgitate in a retrograde direction. Identifying the affected valve is important, particularly now that corrective surgery for certain valvular deformities is a practical reality. Each valve functions under different conditions and is more likely to be affected by one cause of deformities than another. Thus the mitral valve is by far the most common site of rheumatic valvular heart disease, and the incidence of involvement is much lower in the aortic, tricuspid and pulmonary valves, in that order. Cardiovascular syphilis produces aortic incompetence as an isolated valvular lesion. The pulmonary valve is most commonly deformed during embryologic development (see also Chapter 19). Tricuspid valves are rarely affected by either acquired or developmental heart disease.

The necessity for accurate diagnosis of valvular disease will continue to increase as more specific types of therapy are developed for the various lesions. Recent developments in remedial surgery for valvular disease have not only stimulated interest in the problem of diagnosis but have also provided new dynamic information regarding the function of diseased valves in living hearts. In view of the recent drastic change in attitude toward these lesions, particular attention will be directed to the newer concepts. Although mitral valvular disease is the most common, the entire subject can be discussed more coherently by leading off with lesions of the aortic valve.

INCOMPETENCE OF THE AORTIC VALVE

Aortic insufficiency with regurgitation results primarily from either syphilitic aortitis or rheumatic valvular disease.[1] Pure aortic regurgitation is characteristically caused by dilatation of the aortic ring associated with syphilitic aortitis. The valve cusps may remain normal, but as the circumference of the aorta increases, the commissures between the valve cusps widen until they can no longer come into apposition (Fig. 1). Under these conditions, blood is freely ejected into the aorta during left ventricular contraction, but some of this blood regurgitates into the left ventricle during diastole. The incidence of pure aortic regurgitation due to cardiovascular syphilis is being reduced by the recent rapid strides in the detection and therapy of luetic infections. Rheumatic disease of the aortic valves usually produces both stenosis and insufficiency. However, a surprisingly high incidence of rheumatic aortic insufficiency without functionally significant stenosis has been discovered during cardiac surgery. From the functional point of view, aortic incompetence represents a fairly clear-cut volume load and on this basis will be considered in some detail. The fundamental principles which can be clearly visualized in this relatively uncomplicated lesion also apply to many other conditions imposing a volume load on the left ventricle.

The quantity of blood gushing back from the root of the aorta into the relaxed left

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Ventricular Compensation to Pure Aortic Regurgitation

Pressoreceptor mechanisms tend to maintain mean arterial blood pressure within a narrow range. Compensation for depressed diastolic pressure in the arteries involves a marked increase in systolic pressure to maintain a normal mean arterial pressure (Fig. 1) because the duration of the systolic peak is much shorter than that of the diastolic runoff (see Fig. 6, Chapter 10). Such changes in the arterial pressure pulse accompany rather severe grades of aortic insufficiency.

The cardiovascular controlling mechanisms tend to adjust the cardiac output to meet the oxygen requirements of the body as a whole (see Chapter 6). The blood which flows back into the left ventricle during diastole does not contribute to oxygenation of tissues. Therefore, the quantity of blood ejected by the left ventricle must equal the normal cardiac output plus the volume which regurgitates back through the aortic valves. Theoretically, an increased heart rate could augment the cardiac output, but tachycardia reduces the efficiency of the left ventricle. Further, tachycardia would cause a more frequent repetition of the large regurgitant flow in early diastole, increasing the total energy waste. So long as the left ventricle remains competent, the heart rate remains within normal limits. Thus, the principal compensation for aortic regurgitation is a sustained increase in stroke volume sufficient to compensate for the total volume of the regurgitation. The increased stroke volume ejected at a rapid rate accounts for the tall systolic pressure peak in Figure 1.

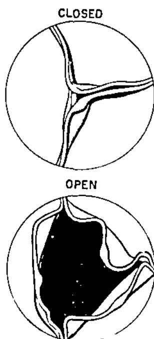
The left ventricle is not architecturally designed as a volume pump because the chamber has a small surface area per unit volume (see Chapters 1 and 7). In response to the continuous requirement for large stroke volumes, the left ventricle dilates and assumes some of the functional characteristics of the right ventricle (Chapter 8). The surface area of the chamber increases markedly, and the degree of myocardial shortening required to eject a particular volume of blood is thereby diminished (Chapter 7). Aortic regurgitation uncomplicated by aortic stenosis produces the most massive left ventricular dilatation encountered in clinical medicine. As the left ventricle becomes distended, the myocardial fibers describe circles of progressively larger diameter and therefore must exert more tension to elevate intraventricular pressure to a particular level. Systolic arterial and left ventricular pressures are higher than normal. The requirement for increased myocardial tension is met by myocardial hypertrophy. For these reasons, massive left ventricular dilatation with a lesser degree of hypertrophy is the usual left ventricular response to uncomplicated insufficiency of the aortic valves.

The characteristics of myocardial contraction are also altered in the face of a sustained increase in stroke volume. The left ventricular adjustments to experimentally induced aortic insufficiency were analyzed by Wiggers.[2] The cardiac response varied with the size of the aperture. Small degrees of aortic regurgitation were accompanied by shortening of the isometric phase of contraction because the diastolic pressure in the aorta was diminished. In other words, ventricular ejection was accelerated because the diastolic arterial pressure was subnormal. Further, the summit of the left ventricular pressure pulse was attained very promptly. When the aortic leaflets were spread wide apart, no significant pressure difference was maintained between the aorta and the left ventricle. Thus, the arterial pressure dropped precipitously during the latter part of systole, roughly paralleling the pressure drop in the left ventricle. Such severe aortic insufficiency is not encountered clinically because it cannot be compensated for long periods.

Effects of Aortic Insufficiency on Coronary Blood Flow

In the normal individual most of the coronary blood flow occurs during ventricular

INCOMPETENCE OF AORTIC VALVE



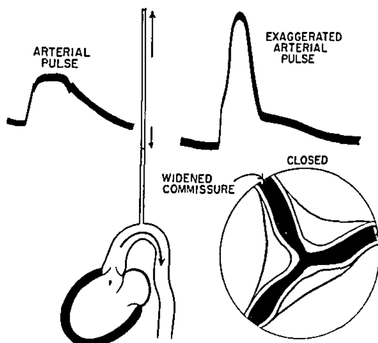


FIGURE 1 *A* The normal aortic valve completely seals off the aortic orifice during diastole and opens to expose a large triangular aperture during ventricular ejection (after McMillan I K R Daley R and Mathews M B The movement of aortic and pulmonary valves studied post mortem by colour cinematography Brit Heart J 14 42–46 1952)

B Pure aortic incompetence usually results from dilatation of the aortic root due to syphilitic aortitis which produces widening of commissures and incomplete closure of the valves Free regurgitation of blood back into the relaxed left ventricular chamber causes the arterial pressure to drop precipitously to low levels during diastole The stroke volume is increased by the amount of the reflux and the systolic peak of pressure is greatly elevated to maintain a normal mean arterial blood pressure Thus the arterial pulse pressure is exaggerated The abnormally great volume load produces dilatation of the left ventricle

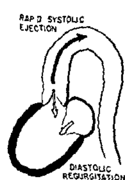
ventricular chamber depends upon the effective pressure difference and upon the area of the unprotected spaces between the valve cusps Large volumes of blood may reflux through relatively small slits between the valve cusps because the pressure difference across the defect is very great (e g the left ventricular pressure may be 10 mm Hg when the aortic pressure is over 100 mm Hg in early diastole) During diastole, arterial blood pressure falls as blood leaves the systemic arterial tree through the peripheral capillaries The rate at which the diastolic pressure falls is determined primarily by the rate at which blood leaves the arterial system in relation to arterial distensibility This fact is somewhat obscured by reflected pressure waves in the arterial system (see Fig 3, Chapter 10) If an additional increment of blood leaves the aorta through defective aortic valves the diastolic pressure drop is accelerated A small quantity of blood surging back through narrow slits between the aortic valves produces little change in the arterial pressure pulse In contrast the arterial pressure falls precipitously if a large volume of blood regurgitates through a gross aortic defect In this case most of the reflux into the left ventricle is completed early in diastole because the driving force diminishes as arterial pressure falls In any case regurgitation is greatest at the beginning of diastole The quantity of blood returning to the left ventricle during each diastolic interval varies widely but may exceed 50 per cent of the total ventricular stroke volume

ejection into the aorta Syphilitic aortitis characteristically produces dilatation of the ascending aorta which would tend to accentuate turbulence initiated by the rapid flow of blood through the aortic valve ring (see Fi 15C Chapter 13)

Presystolic murmurs closely resembling the ausculta ory si ns of mitral stenosis may be heard near the apex of the heart in patients with pure aortic regurgitation (Austin Flint murmurs) Such presystolic apical murmurs have been attributed to the regurgitant stream of blood impinging upon the anterior mitral valve leaflet and pushing it laterally into the atrioventricular blood stream Actually only a small minority of patients with aortic regurgitation have the Austin Flint type of murmur Gouley[7] described a peculiar sagging of one aortic valve cusp (right anterior) so that it presents a concave cup-shaped deficiency facing the anterior mitral curtain in patients with Austin Flint murmurs He thought that this type of aortic valve deformity deflected the regurgitant stream toward the anterior mitral leaflet on which thickening could be demonstrated Such a mechanism might displace the mitral cusp toward a position of closure and produce a murmur simulating mitral stenosis Although such a mechanism might cause a murmur in early diastole when the stream of regurgitating blood has maximal velocity, Austin Flint murmurs occur in late diastole when the arterial blood pressure is minimal and the regurgitation is correspondingly reduced Austin Flint murmurs may disappear as the left ventricle responds to digitalization with diminution in size This observation brings up the possibility that the presystolic murmur is related to immobilization of the mitral valve cusps by ventricular dilatation through tension transmitted by the chordae tendineae This mechanism has been discussed in relation to the diastolic murmurs of acute myocarditis (Fig 9A Chapter 17)

SIGNS OF AORTIC INCOMPETENCE

A BLOOD FLOW



B MURMURS AND PERIPHERAL PULSE

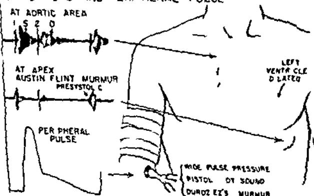


FIGURE 2 4 During systole the left ventricle rapidly ejects an abnormally large quantity of blood into the aorta where the diastolic pressure is abnormally low During diastole the left ventricle is filled with blood entering from both the left atrium and the aorta

B A systolic murmur *over the aortic* area on the precordium probably results from turbulence produced by the very rapid ejection of blood into the aorta The *diastolic* murmur represents the turbulence of a high velocity flow of blood regurgitating through the incompletely closed aortic valves (see also Fig 18 Chapter 13) At the apex of the heart, displaced downward and to the ri ht by massive left ventricular dilatation a presystolic murmur may be heard in a small percenta e of patients Th s Austin Flint murmur may be confused w th a similar murmur heard during mitral stenosis (see Fig 9) The widened pulse pressure may be demonstrated by sphygmomanometry The arrival of the heightened pressure pulse under the stethoscope may produce a loud "pistol shot" sound, Duroziez s murmur consists of systolic and diastolic sounds and is elicited by applying pressure over an artery with the bell of the stethoscope

A single case exhibiting all the characteristic signs of aortic regurgitation is exceptional any or all of these manifestations may be absent or atypical in any particular individual with this lesion.

diastole because the effective pressure in the coronary vessels is greatest during this interval. Severe aortic regurgitation depresses the diastolic pressure in the aorta and perfusion of the coronary vessels should be reduced. However, patients with pure aortic insufficiency rarely have signs of myocardial ischemia unless the coronary ostia are obstructed by the disease process. Presumably the deficit in diastolic coronary flow is compensated by vasodilatation.

Diagnostic Signs in Pure Aortic Incompetence

ALTERATIONS IN THE PERIPHERAL ARTERIAL PRESSURE PULSE. Severe aortic regurgitation produces alterations in the peripheral pulse which explain certain of the condition's characteristic clinical signs. The abrupt ejection of a large ventricular stroke volume into the aorta rapidly elevates systemic arterial pressure to abnormally high levels and causes a pulse wave with a very steep front (Fig. 1).

The changes in arterial pulse contour can be observed on direct arterial pressure records[3] and may be indicated by electrokymography.[4] In severe aortic regurgitation the dicrotic notch disappears and the pressure drops to abnormally low levels during early diastole. The vigorous, bounding pulse wave strikes the palpating finger on a peripheral artery with great force, particularly if the patient's arm is elevated over his head (*vide infra*). This so-called "water-hammer" or Corrigan" pulse develops whenever there is a low resistance run-off from the arterial system (A-V shunts, patent ductus arteriosus or even extreme peripheral vasodilatation). In all these conditions the left ventricle rapidly ejects blood into a systemic arterial system in which the diastolic pressure is abnormally low.

Through a stethoscope positioned over a peripheral artery, one can hear a sharp "pistol-shot sound due to the steep wave front of the arriving pulse. If the bell of the stethoscope is pressed against the artery, turbulence of the blood in the constricted segment produces a murmur during both systole and diastole (Duroziez's sign). Luisada[5] emphasized the fact that the double murmur of Duroziez occurs in many situations producing low total peripheral resistance other than aortic insufficiency. Although the diastolic component of the sound in the peripheral artery is often attributed to a retrograde flow of blood toward the heart, evidence indicates that this vibration is due to a second onward acceleration in flow due to a dicrotic wave of pressure passing under the stethoscope. It is not heard when a dicrotic wave is absent. The changes in the peripheral pulse may not be detected unless the degree of aortic regurgitation is rather severe. Mayne[6] recently observed that if the blood pressure is determined with arm elevated over the head, the diastolic pressure is more than 15 mm. Hg lower than that obtained at heart level. He attributed this greater drop in diastolic pressure to acceleration of the regurgitation by the increased hydrostatic pressure when the brachial artery is oriented vertically over the head, and recommended this test as a means of recognizing mild or moderate degrees of aortic insufficiency which cannot be detected by routine clinical methods.

AUSCULTATORY SIGNS OF AORTIC REGURGITATION. Characteristic systolic and diastolic murmurs are generally heard in the aortic area (second right intercostal space) or in the third left intercostal space. The diastolic murmur is presumably due to the turbulence in the stream of blood as it rushes back through the restricted aortic orifice into the dilated left ventricular chamber (see Fig. 18C, Chapter 13). This murmur has a relatively high frequency and may be difficult to distinguish when its intensity is slight. The diastolic vibrations usually begin as soon as left ventricular pressure drops below aortic pressure immediately after the second sound. If the murmur is sufficiently intense it may be transmitted toward the apex.

The systolic murmur is probably due to turbulence in the blood during the rapid

below the aortic valve this condition also obstructs outflow and is called "subaortic stenosis"

Acquired aortic stenosis has been attributed to two different etiologic factors but recurrent rheumatic valvulitis is generally accepted as the principal cause of valvular stenosis and regurgitation Many aged patients have a marked calcification of fibrotic valves which appears to represent extension of arteriosclerotic changes into the valve cusps and is termed "Monckeberg's aortic valvular sclerosis" Karsner and Koletsky[8] analyzed 200 such cases and concluded that with rare exceptions calcific disease of the aortic valve is actually a manifestation of old rheumatic heart disease Repeated rheumatic infections produce progressive adhesion of the cusps at their commissures which eventually causes stenosis of various degrees The fibrotic valves may calcify as the patient grows older Owing to shrinkage and retraction of the valve cusps with curling of the edges the affected aortic valves are usually more or less incompetent Thus the typical case of rheumatic or calcific aortic valvular disease presents a picture of combined aortic stenosis and aortic insufficiency with one or the other factor predominating Studying the appearance of signs and symptoms during the evolution of calcareous aortic stenosis over periods of 2 to 20 years Boas[9] found that 7 of 15 patients had signs of aortic insufficiency as well

Bailey et al[10] described two principal patterns of rheumatic aortic stenosis In one form vegetations and inflammatory reactions developed uniformly along the lines of valve closure of each cusp so that the cusps adhered along the edematous commissures beginning near the point of their insertion and progressing toward the lumen of the aorta When the process involved the three commissures equally the valve orifice was reduced to a small triangular area in the center of the aortic ring Since the normal aortic valves do not open to the full caliber of the aorta the functional difference between normal and stenotic valves may not be as great as the difference in their appearance at postmortem examination (compare Figs 4A and 1 I) Thus moderate degrees of aortic stenosis may have relatively slight functional effects on the heart Intense fibrosis makes the edges of the valve cusps so stiff that this orifice probably remains open during diastole In these cases slight degrees of insufficiency complicate the stenosis If the aortic lumen is reduced to a small aperture no serious degree of regurgitation occurs even if the valves are completely immobile Thus severe aortic stenosis precludes serious aortic regurgitation Conversely free aortic regurgitation cannot occur with significant aortic stenosis In most patients with aortic valvular disease caused by rheumatic fever, either aortic stenosis or aortic insufficiency will tend to predominate If aortic regurgitation is the principal functional effect the signs and symptoms resemble those encountered in syphilitic aortitis More frequently, the main functional disturbance is obstruction of blood flow from the left ventricle into the aorta

Another common type of aortic stenosis is unequal fusion of the three commissures Usually the two anterior leaflets are so completely fused together that the aortic valve is functionally bicuspid The conjoined anterolateral valve cusps occupy two-thirds of the circumference of the aortic valve ring and act as an unyielding membrane partitioning most of the aortic orifice So long as the posterior leaflet retains its flexibility and motility the remaining aortic orifice opens fairly wide and usually closes completely without regurgitation For purposes of this discussion attention will be directed primarily to aortic stenosis uncomplicated by functionally significant incompetence

Functional Significance of Uncomplicated Aortic Stenosis

In the normal person, the systolic pressure in the left ventricle is but slightly greater than the pressure in the root of the aorta

Systolic murmurs heard at the apex may be due to transmission of vibrations from the aortic valve or from relative mitral insufficiency. If the left ventricle becomes massively dilated, the mitral valve ring may expand until the mitral valve cusps cannot completely cover the orifice. As the left ventricular pressure rises, blood is forced back into the left atrium through a narrow slit or orifice and produces loud systolic vibrations. When the aortic valvular heart disease is caused by rheumatic fever rather than syphilis, structural deformities of the mitral valves should be considered (*vide infra*).

ROENTGENOGRAPHIC SIGNS. Massive enlargement of the left ventricle is readily observed by roentgenography in patients with severe aortic regurgitation. When the valvular defect is slight, the cardiac silhouette often remains normal and the auscultatory signs may be the principal clues to the diagnosis. Dilatation of the ascending aorta may be recognized in the right anterior oblique position or in the left anterior oblique position in which the entire aortic arch may be visualized (see Fig. 2*A*).

ELECTROCARDIOGRAPHIC SIGNS. The principal alterations in the electrocardiogram indicate left ventricular preponderance (see Figs. 19 and 21, Chapter 15). Left axis deviation is very frequently observed, and intraventricular block with left ventricular delay is quite common in advanced cases (see Fig. 25*B*, Chapter 15). Changes in the precordial leads usually confirm the other signs of left ventricular enlargement. Electrocardiographic evidence of myocardial ischemia or infarction is remarkably rare considering the age of most of the patients and the multiple factors which could interfere with coronary flow.

Therapy of Aortic Insufficiency

Surgical repair of valvular insufficiency has always been thwarted by the difficulty of fabricating a valve which even remotely reproduced the permanence, toughness and pliability of the normal valve cusps. While seeking a substitute for segments of major arteries, Hufnagel[1] found that tubes of methyl-methacrylate (Plexiglas) could be used. He developed an artificial plastic valve for use on patients with severe aortic insufficiency. By installing the valve just distal to the left subclavian artery, he eliminated occlusion of the cerebral blood supply during the operation (Fig. 3). He expressed the opinion that 75 per cent of the reflux through incompetent aortic valves could be controlled by an artificial valve in this position. The effectiveness, permanence and desirability of this technique remain questionable.

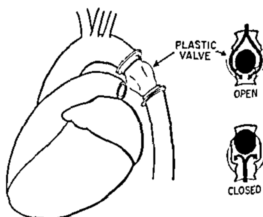


FIGURE 3. A plastic ball valve has been installed in the aortic arch to alleviate aortic regurgitation (after Hufnagel[1]). Rapid developments in cardiac surgery promise continued improvement of valvular prostheses including the use of valves constructed from viable tissues.

AORTIC STENOSIS

Obstruction of the outflow tract of the left ventricle is usually produced by either of two principal etiologic factors: (*a*) congenital aortic or subaortic stenosis and (*b*) rheumatic aortic valvulitis. Congenital deformities of the aortic valve include bicuspid valves or unequal size and position of the three valve cusps. Bicuspid valves of the type occurring in the aorta obstruct the outflow tract to some degree even if the valve cusps are normally pliable (see Fig. 4, Chapter 13). Another congenital defect is the presence of a fibrous band or membrane about 1 cm

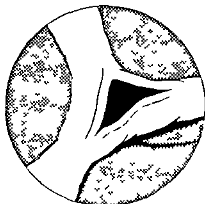
amount sufficient to maintain a normal stroke volume in spite of the increased resistance to outflow (Fig 4D) This is the major functional effect of aortic stenosis

LEFT VENTRICULAR RESPONSE. So long as the area of the aortic orifice is more than half the normal the increase in left ventricular pressure is functionally insignificant The appearance of systolic murmurs in the aortic area from this cause precedes the development of significant stress on the left ventricle often by many years (*vide infra*) As the aortic stenosis becomes more severe the left ventricle responds to a sustained pressure load primarily by myocardial hypertrophy The myocardial fibers must generate greater tension to produce the higher intraventricular pressure during systole Dilatation of the ventricle would be deleterious under these conditions because the myocardial tension would have to increase even more as the fibers described circles of larger and larger circumference Thus the myocardial fibers increase in diameter and the ventricular wall thickens In the early stages of the disease heart size usually remains within normal limits although the contour of the left border may appear rounded in roentgenograms of the posteroanterior view presenting the picture of concentric hypertrophy (Fig 11 Chapter 11) Left ventricular enlargement usually develops in advanced stages of the disease indicating that the myocardium has suffered a loss of contractility The greater the enlargement of the chamber the higher the myocardial tension required Impairment of myocardial function in the left ventricular wall results ultimately from the sustained load on that chamber and coincident myocardial ischemia More than 90 per cent of the useful work of the normal left ventricle represents energy released in the form of pressure energy (see Chapter 8) Ventricular hypertension imposes a very great additional requirement for energy output by the contracting ventricular myocardium The greater energy release requires more rapid delivery of oxygen to the myocardium when in fact aortic stenosis interferes with coronary blood flow

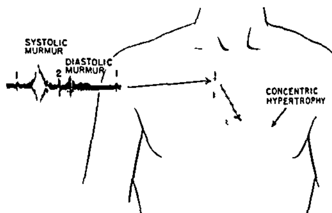
EFFECTS ON CORONARY BLOOD FLOW The quantity of blood perfusing the coronary arteries depends upon (*a*) the pressure gradient from the root of the aorta to the coronary veins and (*b*) the resistance to flow through these vessels which depends upon the caliber of the vessels In the normal heart coronary blood flow is markedly diminished during ventricular contraction because the extravascular pressure compresses the coronary vessels In advanced aortic stenosis the intraventricular pressure greatly exceeds the pressure in the coronary arteries during each systolic interval By this mechanism intramural coronary vessels are emptied and systolic coronary flow is greatly retarded Coronary blood flow should be normal or increased *during* diastole unless the coronary ostia are obstructed by an arteriosclerotic process The increase in the diameter of the myocardial fibers increases the diffusion distance between the blood and the center of each cell which would tend to retard the local delivery of nutrients and the elimination of metabolites (see Fig 6 Chapter 8) Thus aortic stenosis requires an increase in the energy release of the left ventricular myocardium and simultaneously interferes with coronary blood flow while diffusion of oxygen is retarded by hypertrophy of the muscle fibers Under these circumstances one would anticipate a high incidence of myocardial ischemia and infarction Actually precordial and anginal pain does occur but the incidence is quite variable in reported statistics ranging from 10 to 42 per cent of patients About half of the patients with advanced aortic stenosis expire after one or more episodes of congestive heart failure Relative myocardial hypoxia and ischemia no doubt play a role in diminishing myocardial contractility even though myocardial infarction occurs in a relatively small proportion of such cases

STENOSIS OF AORTIC VALVE

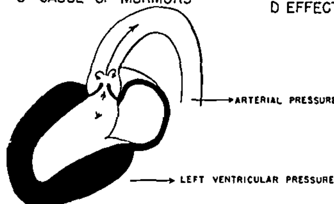
A AORTIC STENOSIS



B DISTRIBUTION OF MURMURS



C CAUSE OF MURMURS



D EFFECTS ON PRESSURES

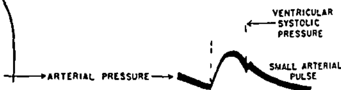


FIGURE 4 *A* Aortic stenosis usually results from rheumatic valvulitis which produces adhesions of the commissures In advanced stages of this process the triangular orifice is rigid so that it impedes systolic ejection and allows regurgitation

B A murmur with maximum intensity in mid systole usually results from the aortic stenosis Incompetence of the aortic valve allows regurgitation producing a diastolic murmur These murmurs are generally distributed along a line connecting the aortic area with the apex of the heart and may simulate the murmurs of pure aortic incompetence (see Fig 2) However the heart is not greatly enlarged unless heart failure supervenes Instead the left border of the cardiac silhouette is often rounded owing to concentric hypertrophy of the left ventricle

C The systolic and diastolic murmurs result from turbulence induced by high velocity blood flow impelled by large pressure gradients across a restricted orifice

D The ventricular pressure pulse is abnormally elevated to provide a pressure head sufficient to force the normal increments of blood past the stenotic valve The arterial pulse pressure is sometimes diminished when the aortic stenosis is severe Clinical signs often fail to indicate whether stenosis or incompetence predominates in any particular patient with rheumatic aortic valvular disease

Very small pressure gradients are required to propel large volumes of blood through large bore tubes Aortic stenosis reduces the caliber of the channel at the junction between the left ventricle and the aorta If the area of the aortic orifice is reduced by some 50 per cent, the normal quantity of blood can be ejected if the pressure drop between the left ventricle and the aorta is only slightly greater However, if the size of the aortic orifice is reduced further, steep pressure gradients are needed to force the normal quantity of blood into the aorta The mean systemic arterial pressure remains within normal limits under the influence of reflexes initiated by pressoreceptors (see Fig 7, Chapter 5), while the cardiac output is also maintained within normal limits being regulated to provide for the oxygen consumption of the body Thus, the systolic pressure developed by left ventricular contraction must exceed the pressure in the aorta by an

aortic area the load on the left ventricle is markedly diminished even though a loud systolic murmur persists The principal dangers of the maneuver are (*a*) fatalities during and immediately after surgery and (*b*) accentuation or production of functionally significant aortic regurgitation Improved operative techniques and more accurate diagnoses should materially improve the outlook in the future

SURGICAL THERAPY OF AORTIC STENOSIS

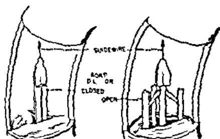


FIGURE 5 One type of aortic commissurotomy is accomplished by means of the Bailey aortic dilator [11] A guide wire is inserted through the left ventricular wall and through *the aortic* valve The dilator is advanced along the guide wire until it is *positioned* within the aortic orifice Three parallel blades are simultaneously forced away from the central column to fracture the *commissures* *Often* only one or two of the commissures are separated by this technique but considerable symptomatic relief is usually attained even if the commissurotomy is incomplete

MITRAL STENOSIS

The clinical signs and symptoms of *mitral* valvular disease should be considered in terms of the functional stresses imposed by the deformed valves and the compensatory mechanisms evoked in response to the load imposed on the circulatory system Although mitral stenosis and regurgitation frequently occur together analysis is simplified by discussing them individually

Functional Anatomy of the Normal Mitral Valve

The anatomic relations of the *mitral* valve were considered in Chapter 13 The structure and functions of *the mitral* valve in health and disease play such an important role in establishing the clinical signs and symptoms of mitral valvular disease that the specific functions of the various component parts are currently receiving renewed attention [1] [15] Brock[15] proposed a greatly simplified functional description of the relation of the valves chordae tendineae and papillary muscles The central portion of each mitral cusp is relatively unsupported by chordae tendineae On either side of this central area (about 1 cm from the midpoint) are the attachments of the thicker and stronger chordae tendineae which lie in the line of direct pull from the tip of the corresponding papillary muscles These four sturdy tendons, two for each valve cusp form the principal support for the central portion of the closed valve at the *critical areas of tendon insertion* According to Brock, these critical areas have particular significance in the development of mitral stenosis (*vide infra*)

The Development of Mitral Stenosis

When the normal mitral valve is open the valve cusps are separated and the chordae tendineae are spread out like a fan During closure the mitral cusps are held in firm apposition along their margins and the chordae tendineae become roughly parallel The mitral aperture can become *restricted* either by adhesions developing along the areas of contact between opposing valve cusps or by fusion of the chordae tendineae Both of these processes may play a role in the development of mitral stenosis Rheumatic valvulitis most commonly produces thickening and fusion of the valve cusps from the region of the commissures toward the center of the mitral orifice The edges of the cusps become thick fibrotic and irregular Viewed from the atrial side the normally flexible valve is converted into a thickened funnel shaped structure with a restricted *orifice* located eccentrically in the mitral ring (Fig 6B) The degree of rigidity of the deformed mitral valve depends on the distribution of the *thickening* and fibrous proliferation The restricted orifice caused by commissural adhesions impedes the flow

Diagnosis of Aortic Stenosis

AUSCULTATORY SIGNS Forceful ejection of blood through a restricted orifice in the aortic valves produces turbulence and vibrations during systole However, constriction of the orifice by only 15 to 30 per cent is enough to create audible vibrations [2] A systolic murmur may be present for years before the aortic stenosis is sufficiently developed to impose any significant functional load on the left ventricle The characteristic *murmur of aortic stenosis is loud* and rough and is transmitted along the great vessels toward the neck and toward the apex of the heart These characteristics permit differentiation of such murmurs from the higher-pitched blowing murmurs of "functional" origin which may be heard in the aortic and pulmonary area Pure aortic stenosis does not produce a diastolic murmur However, many patients with rheumatic aortic stenosis have both systolic and diastolic murmurs even though regurgitation is not functionally significant

EVIDENCE OF LEFT VENTRICULAR HYPERTROPHY In its early phases aortic stenosis usually produces no roentgenographic signs *of left ventricular enlargement* Electrocardiographic signs of left ventricular preponderance appear in most cases The roentgenographic picture of concentric left ventricular hypertrophy may be seen in many such patients If the left ventricle becomes incapable of effectively carrying the load the outflow tract of the left ventricle becomes elongated (Fig 10, Chapter 11) When left ventricular dilatation occurs in a patient with predominant aortic stenosis the clinical picture closely resembles that of aortic insufficiency unless the characteristic changes in the peripheral arterial pulse can be demonstrated

CHANGES IN THE ARTERIAL PULSE The arterial pressure pulse is normal until aortic stenosis becomes sufficiently extensive to seriously retard ejection of blood from the left ventricle When ejection into the aorta is slowed, the amplitude of the pulse wave is diminished The pulse pressure may be reduced so that the peripheral pulse feels weaker than normal The reduced pulse pressure and weak peripheral pulse of aortic stenosis should be easily differentiated from the opposite effects observed with aortic regurgitation Severe aortic stenosis and free aortic regurgitation can often be distinguished on this basis However, combined aortic stenosis and regurgitation often results in a normal pulse pressure without distinctive changes in the peripheral pulse

Combined Aortic Stenosis and Insufficiency

Rheumatic valvulitis often produces both stenosis and insufficiency The functional significance of the stenosis or the regurgitation cannot be estimated from the intensity or character of the murmurs

The systolic murmur of aortic stenosis usually develops maximal intensity in mid systole and the diastolic murmur is loudest in early diastole (Fig 4*C*) Free aortic regurgitation without stenosis (luetic aortic valvular disease) also causes systolic and diastolic murmurs, but in this disease the loudest vibrations often occur early in the systolic interval *In spite of theoretical differences* the murmurs of pure aortic insufficiency and of aortic stenosis with slight regurgitation often cannot be differentiated

Surgical Therapy of Aortic Stenosis

The principal functional disturbances in aortic valvular stenosis can be largely eliminated by alleviating the abnormal resistance to left ventricular ejection Bailey and his co-workers[10 11] have *developed a method* for separating the fused cusps of the aortic valve by means of a specially designed dilator (Fig 5) The results of this type of therapy are very promising and the approach has a sound physiologic basis The most rewarding aspect of aortic commissurotomy is the fact that symptomatic relief and functional improvement can often be obtained even when the separation of the valve cusps *is incomplete If the obstruction* can be reduced to less than 50 per cent of the normal

mitral orifice could seal completely during systole Fibrinous excrescences such as those illustrated in Figure 2 Chapter 17 may extend as webs or diaphragms down between chordae tendineae and later organize into fibrous tissue lengthening the valve cusps Both the valve cusps and the chordae tendineae may be involved to varying degrees by three processes (*a*) fusion, (*b*) thickening and proliferation and (*c*) retraction or shortening A wide variety of end results can evolve from combinations of these three processes distributed unequally within the various portions of the valve and its adnexa

In contrast to generally accepted concepts Brock[15] suggested that fusion of the valve cusps begins near the insertion of the strongest chordae tendineae at the two opposing critical areas of tendon insertion If adhesions developed at these areas the hinge action of the valves would be immediately impaired since the central channel could not open widely Even if the valve edges toward the periphery from these areas remained separate they could not open widely and would probably become fused too

Further evidence cited for this concept includes the fact that the mitral valve orifice is rarely greater than 1 5 by 0 75 cm and rarely smaller than about 1 by 0 5 cm The relative constancy of the valve aperture in mitral stenosis has been noted by Gorlin and Gorlin[17] and by Janton et al [18] but it could be explained on other grounds (e g surgery is rarely indicated unless the mitral valve reaches 1 5 by 0 75 cm and survival may not be common if the orifice is smaller than 1 by 0 5 cm)

Functional Effects of Mitral Stenosis

The pressure gradient required to maintain a constant flow of fluid along a channel depend largely upon its caliber The channel from the left atrium to the left ventricle is normally so spacious that the diastolic pressure gradient is difficult to demonstrate with available techniques Since mitral stenosis is a local constriction at the mitral orifice, a greater pressure gradient is needed to sustain left ventricular filling An increase in the pressure drop across a restricted mitral orifice represents a very large increase in the frictional energy loss in the flowing blood Some of this energy loss is due to turbulence stemming from the high velocity with which the blood passes through the small aperture into the left ventricular chamber The turbulence usually produces audible diastolic murmurs

Since the work of the left ventricle is either normal or reduced, no ventricular compensation is required and the diastolic pressure is presumably normal Gordon et al [19] found the mean left ventricular diastolic pressure to range between 3 and 11 mm Hg and the end diastolic pressures between 2 and 15 mm Hg The pressure gradient from left atrium to ventricle through stenosed mitral valves varied from 4 to 20 mm Hg before the orifice was expanded surgically and diminished thereafter in direct relation to the adequacy of the dilatation An increased pressure gradient across the stenosed mitral valve requires an increase in left atrial pressure which is reflected back through the pulmonary veins, capillaries and arteries (see Fig 8) Clearly, the principal functional disturbances produced by mitral stenosis are (*a*) increased blood pressure upstream from the site of the obstruction resulting in pulmonary congestion and hypertension and (*b*) turbulent flow through the mitral orifice producing murmurs

Gorlin and Gorlin[17] computed the magnitude of the pulmonary capillary or venous pressures required to provide a particular level of diastolic filling through mitral orifices with various areas (Fig 7) As the area of the mitral valve orifice decreases below 2 sq cm pulmonary pressures must mount higher and higher to maintain a particular level of flow through the valve When the mitral orifice is smaller than 1 sq cm the blood flow is only slightly affected by pulmonary pressures ranging from 20 to 60

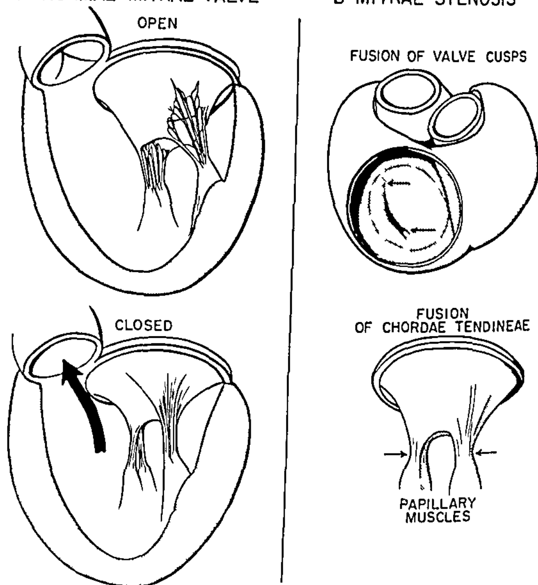


FIGURE 6 *A* When the normal mitral valve is open the valve cusps gap and the chordae tendineae fan out During ventricular systole the valve cusps and chordae tendineae are forced together Any process which holds the valve cusps or chordae tendineae in the closed position during ventricular filling produces mitral stenosis

B Mitral stenosis from recurrent rheumatic fever can result from either fusion of the valve cusps (above) or fusion of chordae tendineae (below) Generally both processes occur in various degrees The normally supple valve cusps tend to be converted into a thickened rigid diaphragm when fusion along the commissures is the predominant deformity If on the other hand adherence of the chordae tendineae is the primary pathologic process the valve cusps may remain fairly flexible

of blood into the ventricles The rigid, irregular valve margins probably fail to seal off the mitral orifice during systole, so that there is some regurgitation through the diseased valves This general type of mitral stenosis occurs in about 85 per cent of patients [16]

If the inflammatory process is concentrated in the chordae tendineae, they become fused together as indicated in Figure 6*B* If the chordae tendineae are inseparably fused, the mobility of the mitral cusps is seriously restricted even if their flexibility is relatively unimpaired [12 15] This process may explain the development of "pure" mitral stenosis with no regurgitation, since the

3 Increased pulmonary capillary pressure calls for increased pulmonary arterial pressure since the normal pulmonary pressure gradient is very low Such pulmonary hypertension imposes a severe pressure load on the right ventricle and produces right ventricular hypertrophy

Some of the effects of mitral stenosis have been confirmed by direct measurements When mitral stenosis becomes severe enough to produce symptoms most patients have some elevation of pulmonary arterial pressure and low normal or subnormal cardiac output at rest During exertion the pulmonary hypertension tends to become greatly accentuated and the cardiac output fails to increase to the normal extent[1, 23] As so frequently occurs in clinical medicine disturbing discrepancies are found between logical theory and direct observations For example Ball et al[2] reported that intrathoracic blood volume in patients with mitral stenosis was no greater than normal even when resting cardiac output was subnormal Direct measurements of pulmonary arterial pressures by cardiac catheterization do not always correlate well with the severity of valvular lesions[21] One cause of such discrepancies is the development of sclerosis in terminal arterial branches in the lungs (*vide infra*)

RESPONSE OF THE LEFT ATRIUM Contraction of the atrial wall reduces the capacity of the chamber and forces blood either into the left ventricle or into the pulmonary veins depending upon which course offers less resistance Myocardial fibers form an investment for the pulmonary veins extending some distance from the atrium Contraction of these fibers should retard retrograde flow and promote forward flow into the left ventricle The retrograde flow of blood into the pulmonary veins is further diminished by the high pressure in the pulmonary veins which greatly reduces their distensibility The atrial musculature must overcome a pressure load to which myocardial hypertrophy is the typical response

EFFECTS OF PULMONARY CONGESTION The pressure gradient from the pulmonary artery to the left ventricle is so slight that any elevation in left atrial pressure is reflected back through the entire pulmonary circuit When the mitral orifice diminishes below some critical level left atrial and pulmonary vascular pressures rise whenever the cardiac output increases The increase in pulmonary pressure within a distensible vascular bed implies that the pulmonary vessels become engorged simulating the effects of left ventricular failure (see Chapter 9)

Dyspnea Quantitative measurements of circulatory and respiratory dynamics in patients with mitral stenosis indicate that the pulmonary congestion frequently decreases both vital capacity and maximal breathing capacity, but not to an extent which would account for the degree of respiratory disability[4] From this type of information it can be inferred that the dyspnea associated with pulmonary congestion in mitral stenosis results predominantly from the reflex mechanisms previously described (see Fig 4 Chapter 9) As stenosis of the mitral valve progresses pulmonary congestion follows smaller and smaller increases in cardiac output until dyspnea appears with mild physical exertion Severe degrees of mitral stenosis result in elevated pulmonary pressures at rest with very great pulmonary hypertension required to produce even slight increases in cardiac output (see Figure 7) Limitation in cardiac output produces fatigue and dyspnea out of proportion to the degree of physical activity

Pulmonary sclerosis Some of the discrepancies between the size of the mitral orifice and the severity of the symptoms may result from pathologic changes in the pulmonary vascular bed Some patients with protracted severe mitral stenosis develop diffuse sclerotic changes in the terminal ramifications of the pulmonary arterial tree The media also becomes thickened by a proliferation of smooth muscle which reduces the lumen of the vessels[25] According to Henry[26] such vascular changes occurred in 40 per cent of his patients with mitral

PRESSURE DROP ACROSS STENOTIC MITRAL VALVES

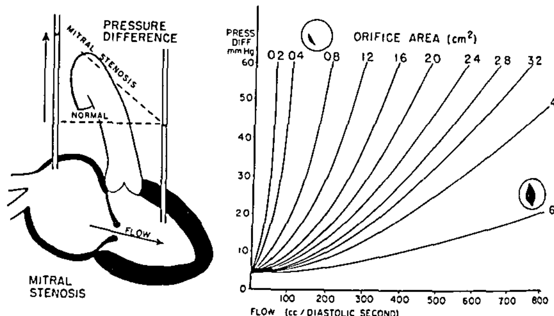


FIGURE 7 Mitral stenosis necessitates a steep pressure gradient to force the normal increments of blood past the restricted orifice between the left atrium and ventricle The magnitude of the pressure difference is related to the area of the effective mitral orifice as indicated by the graph If the mitral orifice is large very rapid ventricular filling can result from a relatively slight increase in left atrial pressure In contrast the flow through extremely small orifices (0 2 or 0 4 sq cm) increases only slightly even when the pressure gradient reaches very high levels (after Gorlin and Gorlin[17]) This graph illustrates the important roles played by valvular orifice area and rate of blood flow in the production of pulmonary hypertension and congestion even though the computations are not universally accepted as quantitatively reliable (see text)

mm Hg Thus, at the smallest orifices illustrated in Figure 7 the flow is almost constant regardless of how steep the pressure gradients become These investigators[17] also estimated the effective area of the mitral orifice from data obtained during cardiac catheterization and found a good correlation between the severity of the symptoms and the size of the mitral aperture (Table 11)

TABLE 11 RELATION OF VALVULAR CROSS SECTIONAL AREA TO CLINICAL SYMPTOMS IN PATIENTS WITH MITRAL STENOSIS

CLINICAL CLASSIFICATION	MITRAL VALVE AREA (CM 2)	NUMBER OF PATIENTS	PHYSICAL ACTIVITY
I	2 5	1	Virtually unlimited
II	1 3–1 6	3	Some limitations
III	0 6–1 1	4	Very limited
IV	0 4–0 9	12	Bed and chair

Considering the intimate relationship between pressure and flow through a restricted orifice the functional effects of mitral stenosis should be predictable

1 Progressive reduction in the area of the mitral orifice should be accompanied by higher and higher left atrial pressure

2 More rapid blood flow (increased cardiac output) should be associated with a further increase in atrial pressure, e g , during physical exertion Severe mitral stenosis should limit the extent to which the cardiac output is increased during exercise

3 Increased left atrial pressure must be accompanied by a corresponding increase in pulmonary venous and capillary pressure producing signs of pulmonary congestion which are accentuated whenever greater cardiac output is required

4 When the pulmonary capillary pressure exceeds the osmotic pressure of the plasma proteins the patients should develop pulmonary edema when the rate of capillary filtration exceeds the lymphatic drainage[20]

tion" occurring in 12 per cent of his patients with mitral stenosis Taquini et al [8] found that 2 per cent of their patients with mitral stenosis followed a downhill course with early development of right ventricular failure which was associated with a very high pressure gradient between pulmonary arterial and pulmonary capillary pressure In these patients high arteriovenous oxygen differences and very low cardiac outputs were demonstrated However Taquini and his co-workers found dyspnea to be particularly pronounced It is difficult to reconcile the prominence of dyspnea described by Taquini and the protection from pulmonary congestion described by Wood in patients who were apparently suffering from the same type of functional disturbance However, it is clear that the sclerosis and spasm of pulmonary arterial branches may produce pulmonary hypertension out of proportion to the severity of the mitral stenosis

Cyanosis Visible cyanosis is commonly seen among patients with advanced mitral stenosis When the alveolar capillaries are distended with blood, the distance for diffusion of gases from the alveoli into the center of the blood stream is increased Thickening of the alveolar walls and accumulation of extravascular fluid would also tend to retard oxygenation of the blood [24] These factors presumably contribute to cyanosis appearing at rest Limited increase in cardiac output requires an increased oxygen extraction and widened arteriovenous oxygen difference in the systemic capillaries during exertion The increased oxygen extraction in the cutaneous capillaries may produce peripheral or stagnant' cyanosis A more comprehensive discussion of cyanosis will be presented in relation to congenital malformations of the heart (Chapter 19)

Hemoptysis Acute profuse hemoptysis occurs in some 10 per cent of patients with mitral stenosis [29] It may appear at virtually any stage of the disease but is more common when the disease process is advanced The source of pulmonary hemorrhage probably lies in the rather unique relation between the bronchial and pulmonary circulations The bronchial arteries are distributed to capillary beds in the walls of the bronchi In most parts of the lungs the bronchial capillaries drain into the pulmonary veins The elevated pulmonary venous pressure is reflected back into the bronchial capillaries, which also become congested (see Fig 4 Chapter 9) Rupture of small distended vessels in the bronchial mucosa is probably responsible for pulmonary hemorrhages and hemoptysis The congestion of bronchial mucosa may also contribute to a productive cough occurring particularly after physical exertion Gilroy et al [30] reported engorgement of pleurohilar veins which drain into the systemic venous system as well as distention of the true bronchial veins in some patients with mitral stenosis

Right Ventricular Failure. The pulmonary arterial pressure is typically elevated by advanced mitral stenosis. Wood's [27] patients with mitral stenosis without significant pulmonary stenosis had mean pulmonary arterial pressures ranging around 35 mm Hg and pulmonary capillary pressures about 20 mm Hg at rest Patients with the so-called protective hypertension had mean pulmonary arterial pressures of 50 to 60 mm Hg The right ventricle must pump against these increased outflow pressures which constitutes a persistent pressure load However the right ventricle is poorly adapted for the role of a pressure pump (see Chapter 8) Thus the terminal stage of mitral valvular heart disease is the advent of right ventricular failure with systemic venous congestion and peripheral edema by the mechanisms described in Chapter 9

Diagnosis of Mitral Stenosis

Most patients are free of symptoms for many years after their final attack of acute rheumatic fever During this period the mitral orifice is presumably progressively restricted and yet exercise tolerance and physical well-being are not apparently affected Among such patients are individuals with remarkable athletic prowess The pre-

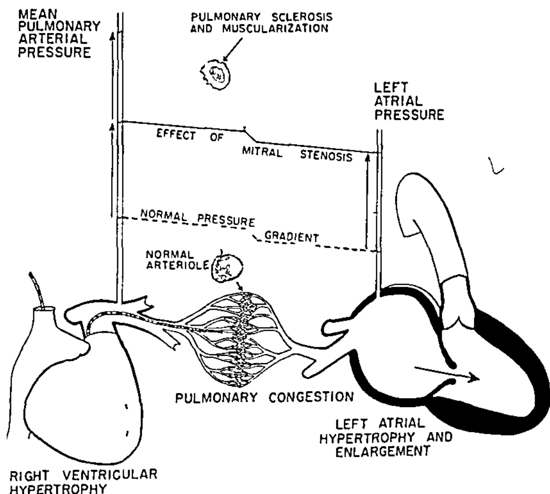


FIGURE 8 The resistance to flow through the normal pulmonary vascular tree is so slight that the gradient in mean pressures from pulmonary artery to left atrium ranges around 4 to 6 mm Hg even at flow rates as high as 10 or 12 l per minute Mitral stenosis produces an elevation in left atrial pressure (see Fig 7) which is reflected back along the entire pulmonary vascular bed When pulmonary vascular pressure increases pulmonary congestion usually follows Sustained pulmonary hypertension appears to stimulate sclerosis and muscularization of the terminal pulmonary arteries and arterioles in about 40 per cent of patients with mitral stenosis (after Henry[26]) and greatly increases the resistance to flow through these narrowed channels in 12 to 20 per cent of such patients The increased pulmonary arterial resistance produces severe hypertension in the pulmonary arteries which imposes an even greater pressure load on the right ventricle Under these conditions pressures recorded through a catheter wedged in a terminal pulmonary artery are much lower than in the main arterial trunk

stenosis and in none of his controls The increased muscularity of the small pulmonary arteries is an expression of their sustained constriction, which produces a drop in the pressure of the blood just before it flows into the pulmonary capillaries Under these circumstances, resistance is markedly increased in two different regions, in the pulmonary arteries and at the mitral valve The pressure drop in the smaller pulmonary arteries diminishes the pulmonary capillary pressure, but also correspondingly diminishes the pressure gradient across the restricted mitral orifice (Fig 8) Patients exhibiting this type of response to mitral stenosis have little or no dyspnea, but their physical activity is severely restricted since the cardiac output tends to remain fixed at the resting level Oxygen consumption is increased almost exclusively by increased oxygen extraction so intense fatigue on exertion is their principal complaint Paul Wood[27] has described this type of response as a "protective pulmonary vasoconstric

of the left ventricle into better contact with the chest wall

These characteristic murmurs of mitral stenosis may first appear many years after the last attack of acute rheumatic fever or having once appeared may regress and disappear completely[34] (Fig 11 Chapter 17) According to Levine and Love[35] 5 to 10 per cent or more of patients with mitral stenosis may have no audible diastolic murmur There is little doubt that mitral stenosis may cause significant vibrations which are below the level of audibility This can often be demonstrated by phonocardiographic equipment[36]

In the past mitral stenosis was rather confidently excluded if no apical diastolic murmurs were audible and was diagnosed with some assurance if the typical apical diastolic rumble was detected In view of recent evidence, neither of these attitudes is justified Diastolic murmurs simulating those of mitral stenosis occur during initial or early attacks of rheumatic carditis and then disappear completely as the patient recovers (Chapter 17) On the other hand patients with definite mitral stenosis may have no audible diastolic murmurs[35,37] Incorrect diagnosis commonly results from excessive reliance on auscultatory signs of either mitral stenosis or mitral regurgitation Auscultation is not a reliable method for assessing the severity of a valvular lesion and frequently fails to indicate which valve is affected by disease The other manifestations of mitral stenosis resulting from increased blood pressure upstream from the obstruction must be considered in conjunction with clinical history and auscultatory signs in arriving at a diagnosis

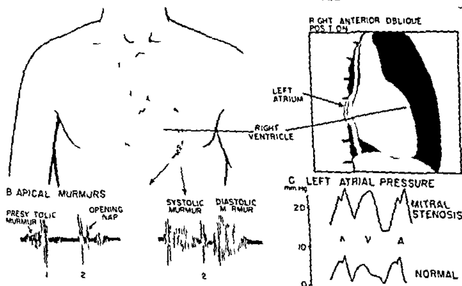


FIGURE 9 A The characteristic change in the cardiac silhouette produced by mitral stenosis is straightening of the left border viewed from the postero-anterior position (due to right ventricular hypertrophy) Left atrial enlargement which occurs much earlier in the disease can best be seen in the right anterior oblique position (see also Fig 12 Chapter 11)

B Auscultatory signs of mitral stenosis include presystolic murmurs which increase in intensity to end in a loud first heart sound the opening snap which is a brief high-frequency vibration occurring about 0 07 second after the second sound a low frequency murmur during diastole and often a systolic murmur (After Wells B G The graphic configuration of apical diastolic murmurs Brit Heart J 14 261–270 1952)

C Direct pressure records from the left atrium demonstrate an elevated left atrial pressure The form of the pressure waves is altered producing a wide variety of patterns but the taller pressure wave during ventricular systole (V) is frequently observed (After Wynn, A Matthews M B McMillan J K R and Daley R 41)

mary symptoms which ultimately develop are dyspnea on exertion and easy *fatigability* from pulmonary congestion and restricted cardiac reserve, respectively Since subjective symptoms often appear late in the disease process, rheumatic valvular heart disease is frequently detected during routine examinations or protracted case studies of patients with known attacks of rheumatic carditis For this purpose, auscultation is the most sensitive test

AUSCULTATORY SIGNS The characteristic auscultatory manifestations of mitral stenosis are (*a*) accentuated first sound at the apex, (*b*) opening snap of the mitral valve, (*c*) accentuated second sound at the pulmonary area and (*d*) diastolic rumble at the apex Not all of these signs are necessarily present in any one patient, and heart sounds and murmurs often change during recurrences of acute carditis (see Chapter 17)

Accentuation of the first sound at the apex The apical first sound is frequently loud and snapping in the presence of mitral stenosis The apparent increase in intensity of the sound may result from the higher frequency of vibration stemming from the more rigid valves

Opening snap In some patients with mitral stenosis, a very brief, high frequency vibration is heard approximately 0 08 second *after the principal elements of the second* sound This characteristic sound has been termed the "opening snap" of mitral stenosis because it seems to occur at the beginning of ventricular filling The opening snap occurs slightly before the instant at which a third heart sound would be heard and can be distinguished from a third heart sound by its relatively high pitch[31] The incidence of the opening snap varies according to different observers but when present, is considered an important auscultatory sign of mitral stenosis Mounsey[3] reported hearing an opening snap in 28 of 33 patients with mitral stenosis and finding phonocardiographic evidence in 4 more This is a much higher incidence than is generally reported The opening snap was heard best at a point just above and medial to the *mammary region at the left* sternal margin and at the mitral area In 31 of 33 patients, Mounsey[32] found both splitting of the second sound and an opening snap The two elements of a split sound occur within 0 07 second, which is very similar to the interval between a second sound and an opening snap Acceleration of the heart rate tends to reduce the interval between the second heart sound and the opening snap[33] The typical diastolic murmur of mitral stenosis usually begins at about the time of the opening snap and the latter sound may persist when the diastolic murmur becomes equivocal or absent

Accentuated second sound at the pulmonary area The second sound in the pulmonary area is intensified when the pressure in the pulmonary artery is high, just as the aortic second sound tends to become louder during systemic hypertension In most patients, other evidence of pulmonary hypertension and congestion can be elicited when the pulmonary second sound is accentuated

Diastolic murmurs The turbulence resulting from a rapid flow of blood through a stenotic mitral valve should produce an audible diastolic murmur Theoretically, this murmur should be most intense during early diastole and during atrial contraction (presystole) *Owing to the obstruction* offered by the narrowed orifice early diastolic filling is probably retarded so that flow persists throughout the diastolic interval In other words the period of slow filling or diastasis is utilized to permit more adequate ventricular filling Thus, the diastolic murmur may persist throughout the entire ventricular filling period, being accentuated in early diastole and during atrial systole (Fig 9) The resultant murmur is a low-frequency vibration or rumble, presumably because the relaxed left ventricular wall has a low natural frequency of vibration The murmur is usually heard best in the vicinity of the precordial impulse, and may be accentuated when the patient lies on the left side This position brings the apical portion

sclerosis the catheter is advanced until it wedges in a pulmonary arterial branch. Under these conditions, the pressure recorded through the tip of a wedged catheter is transmitted in a retrograde direction from contiguous vessels through which blood is flowing. Although such pressures are often termed "pulmonary capillary pressure," they are probably more closely related to pulmonary venous pressures.[42] Simultaneous measurements during cardiac surgery indicate that variations in the pressure in the pulmonary veins and left atrium are quite faithfully reflected in the wedged catheter. In some patients the vigorous atrial contraction produces an accentuated A wave on the records.

The resistance offered by the mitral orifice has been estimated by inserting the values for cardiac output and wedged catheter pressure in the formula $R_m = (PC_m \times 1.332 \times 60)/CO$ where R_m is the resistance offered by the mitral valve, PC_m is mean pulmonary capillary pressure measured by a wedged catheter and CO is cardiac output. Formulae of this type are useful in summarizing data and making comparisons but they are based on some assumptions which may introduce considerable error. For example, the true significance of the pressure recorded from a catheter wedged in a pulmonary artery is somewhat questionable. Further, the formula presented above implies that left ventricular pressure is *zero*. For such reasons, computed values using impressive formulae of this type are often purely qualitative and must not be taken too seriously.[43]

Surgical Therapy of Mitral Stenosis
Mitral Commissurotomy

The most common surgical approach to the mitral valve is through the left atrial appendage (auricle). A purse string suture of braided silk is placed around the base of the auricle after ascertaining that no thrombi are present. An incision of sufficient size to admit the index finger is made in the tip of the auricle. The valve is palpated gently and carefully to determine the severity of the stenosis. If mitral regurgitation is present, a jet of blood striking the finger during systole can be readily perceived. In some 15 to 20 per cent of patients the surgeon discovers mitral insufficiency of such severity that mitral commissurotomy cannot be safely carried out. The difficulties involved in differentiating predominant mitral stenosis and mitral incompetence are considered in the next section. If the stenotic mitral orifice will admit the finger, digital pressure applied along each commissure in turn will usually separate the fused valve cusps. In some patients finger pressure does not fracture the commissural adhesions and a special cutting instrument (valvulotome) is inserted alongside the finger to initiate the commissural separation. If the commissurotomy is successful, a mitral orifice which would admit only a finger tip is expanded to a size sufficient to accommodate three fingers and no additional mitral regurgitation is produced.

The principal contraindications to the operation were enumerated by Hufnagel:[1] (1) active myocarditis, (2) the presence of other functionally significant valvular lesions, (3) severe uncontrolled congestive heart failure and (4) the presence of other disease states with less favorable prognoses than the mitral stenosis. These logical contraindications are deceptively simple and the first two cannot always be recognized preoperatively. For example, signs of unsuspected active carditis (Aschoff nodules in the excised atrial appendage) are found in about 50 per cent of patients undergoing mitral valvulotomy. Most of these adult patients have had no clinical evidence of active carditis for many years. Furthermore, signs suggesting mitral valvular disease occur in patients with aortic or tricuspid valvular lesions. Finally, there seems to be no dependable sign by which predominant mitral incompetence can be consistently differentiated from relatively pure mitral stenosis prior to surgical exploration. Since no technique for remedial surgery on mitral incompetence has been established, detecting

ROENTGENOGRAPHIC SIGNS The changes in the size or shape of the cardiac chambers accompanying mild or moderate degrees of mitral stenosis are usually so slight that no evidence of chamber enlargement can be observed In such patients, the cardiac silhouette appears normal from all angles in spite of the typical murmurs indicating mitral stenosis Left atrial enlargement may not be demonstrable by roentgenographic examination even when it is marked For example, Pariser et al [38] reported that left atrial enlargement could not be demonstrated by fluoroscopy in 6 patients out of 30 who exhibited moderate to gross left atrial enlargement during postmortem examinations In "pure" mitral stenosis, the left atrium may not be enlarged during the early stages,[39] presumably because this chamber compensates for the pressure load by hypertrophy Similarly, mitral stenosis tends to retard left ventricular filling, so that the size of this chamber is usually normal or subnormal in the absence of heart failure, mitral incompetence or aortic disease, etc Thus roentgenographic examination often fails to indicate enlargement of either the left atrium or the left ventricle in pure mitral stenosis Jacobson et al [40] preferred the left lateral to the right anterior-oblique position for the early detection of left atrial enlargement Incompetence of the mitral valve accompanying mitral stenosis leads to dilatation of both the left atrium and the left ventricle (see Fig 10, Chapter 11) Persistent pulmonary hypertension causes right ventricular hypertrophy (Fig 13, Chapter 11) and accentuated pulmonary vascular markings in the lung fields, particularly in the hilar regions

INTRA-ATRIAL THROMBOSIS Mural thrombi are a constant threat in patients with widely dilated atria, particularly when atrial fibrillation persists The most immediate source of danger is systemic embolization, resulting from fragments of the clot lodging in vital organs In some patients, the thrombus progressively enlarges to reach large dimensions and, if strategically located, impedes blood flow through the atrium or through the already stenotic mitral orifice

ATRIAL FIBRILLATION Fibrillation of the atria commonly develops when atrial chambers are enlarged, particularly from mitral valvular disease (see Fig 10, Chapter 14) Among patients with mitral stenosis, the resting cardiac output tends to be lower during atrial fibrillation than during normal sinus rhythm,[21] indicating that a coordinated atrial systole may contribute significantly to ventricular filling

ELECTROCARDIOGRAPHIC SIGNS When the left atrium becomes hypertrophied and dilated, the P waves usually are prolonged and have flattened or notched summits in lead I and to a lesser extent in lead II (see Fig 23, Chapter 15) This pattern is so typical that it is often termed P mitrale even though it may occur in other conditions Reynolds[41] recorded potentials directly from the atria during surgery on patients with mitral stenosis and found that the voltage from the left atrium was increased (see Fig 23, Chapter 15) Asynchronism of right and left atrial excitation was present in all tracings and was increased in patients with mitral stenosis The initial peak is derived from the right atrium and both the delay and the prolongation of left atrial excitation apparently produce the flattened or notched P waves

Persistent pulmonary hypertension with right ventricular hypertrophy results in electrocardiographic evidence of right ventricular preponderance (see Fig 22, Chapter 15)

CARDIAC CATHETERIZATION Pulmonary hypertension can be detected by measuring the pressure through a cardiac catheter introduced into the pulmonary artery Mean pulmonary arterial pressure is often elevated to 25 or 35 mm Hg or more in patients with symptoms from mitral stenosis Much higher pressures occur (over 55 mm Hg) when sclerosis develops in the terminal branches of the pulmonary arterial tree (see Fig 8) To determine the proportion of the pulmonary hypertension due to pulmonary

rush of blood back through the mitral orifice into the capacious atrial chamber produces turbulence perceived externally as a widely transmitted systolic murmur usually with maximal intensity in the apical region. The blood tends to follow the course of least resistance so only a proportion of the total ejection enters the aorta. Thus the stroke volume of the ventricle must be greatly increased to maintain arterial pressure and systemic blood flow. Under such a sustained volume load the left ventricle should distend to much larger systolic and diastolic dimensions. The quantity of blood entering and leaving the left atrial cavity is correspondingly increased so this chamber also labors under a volume load and should become dilated. Contraction of the dilated atrium might be expected to expel an abnormally large quantity of blood increasing the terminal ventricular filling and also displacing a larger quantity of blood backward into the *pulmonary veins*. Furthermore reflux of blood from the ventricle should exaggerate systolic expansion of the atrium which would be associated with a second tall peak of pressure on the atrial pressure curve.

Based on this analysis the principal signs of mitral incompetence should include (*a*) a loud systolic murmur in the mitral area (*b*) dilatation of the left ventricle (*c*) dilatation of the left atrium with augmented expansion during ventricular systole (*d*) exaggerated pulmonary venous pressure waves during both atrial and ventricular systole and (*e*) limited stroke volume and cardiac output reserve leading to fatigability. These symptoms may be clearly manifested in an occasional patient with functionally pure mitral incompetence. However most patients with mitral insufficiency also have some stenosis so the clinical picture becomes complicated.

APICAL SYSTOLIC MURMUR. Functional systolic murmurs can mimic those observed in patients with established mitral insufficiency. Similar systolic murmurs are heard during initial attacks of rheumatic and nonspecific myocarditis and clearly do not indicate functionally significant mitral leakage. They are not usually as loud as those commonly encountered with mitral regurgitation but their characteristics are similar. Surprisingly enough not all patients in whom a retrograde jet is palpated by the exploring finger of the surgeon during cardiac surgery have detectable systolic murmurs. For example Elkin et al[44] reported that 5 of 15 such patients had no systolic murmur. Venner and Holling[45] compared the clinical and surgical findings in 96 patients. Nine patients had widely incompetent mitral valves and systolic murmurs but in one the intensity was no greater than that in persons with functional murmurs. Thirteen of 61 patients without palpable regurgitation had loud apical systolic murmurs. No distinguishing features between the systolic murmurs in patients with and in those without palpable regurgitation were noted. From these observations systolic murmurs appear to be tenuous signs of mitral regurgitation and other evidence must be sought.

DILATATION OF THE LEFT VENTRICLE. In the absence of aortic valvular disease roentgenographic evidence of gross left ventricular enlargement facilitates differentiation of mitral insufficiency and mitral stenosis. In about half the patients with predominant mitral regurgitation the left ventricular contour is not remarkable on either roentgenograms or fluoroscopic examination. Electrocardiograms provide evidence of left ventricular preponderance in about the same proportion and in the remainder right ventricular hypertrophy or combined ventricular hypertrophy may be indicated. Since rheumatic carditis often affects more than one valve left ventricular enlargement can result from either mitral or aortic valvular disease. Other causes for left ventricular enlargement such as heart failure hypertension and myocardial infarction must be kept in mind.

DILATATION OF THE LEFT ATRIUM. The atrium is dilated in a majority of patients with either mitral regurgitation or mitral

mitral regurgitation is particularly important in deciding the feasibility of mitral commissurotomy

MITRAL INCOMPETENCE

In the past, a diagnosis of mitral insufficiency was usually applied when an apical systolic murmur was too loud and persistent to be classified as 'functional' Virtually all patients with acute rheumatic carditis develop systolic murmurs which persist for years With no additional confirmatory evidence, such patients were labeled as having mitral insufficiency Bland and Jones[34] reported the subsequent course of 87 patients with systolic murmurs on discharge from the hospital after their initial attack of rheumatic fever Twenty years later, 7 had mitral stenosis 16 had mitral stenosis with evidence of regurgitation, 35 had mitral regurgitation diagnosed primarily on the presence of the murmur, and 29 no longer had the systolic murmur Clearly, the systolic murmurs so frequently discovered during initial attacks of acute rheumatic fever do not signify significant mitral incompetence Postmortem examinations on such patients are very rare and mitral incompetence cannot be reliably diagnosed by examining an excised heart unless the valvular deformity is severe In most patients, the changes in the valves following acute rheumatic valvulitis are believed to heal quite completely although the systolic murmur often persists On the basis of such evidence the significance of apical systolic mumurs in rheumatic patients deserves reappraisal

Types of Mitral Insufficiency

MITRAL MISFIT Edematous thickening and verrucae, which develop along the valve margins during acute rheumatic fever (see Fig 2, Chapter 17) might prevent complete sealing of the valve cusps during ventricular systole Spurts of blood between such vegetations theoretically could produce prominent systolic murmurs Since reflux of such small quantities of blood would have no appreciable effect on cardiac function it seems unwise to apply the ominous diagnosis of mitral incompetence thus, the term "mitral misfit" is used above However, these vegetations are largely resorbed after the acute phase of the disease has passed The patients who are routinely classified as cases of pure mitral insufficiency on the basis of systolic murmurs at the apex have little functional disability for many years Judging by indirect experimental evidence such patients might have no mitral regurgitation at all (see Fig 7, Chapter 17)

FUNCTIONALLY SIGNIFICANT MITRAL REGURGITATION When mitral incompetence is encountered during cardiac surgery in adults the valves have frequently become so fibrous and rigid that they resist both opening and closing Even if the valves retain some flexibility, they may be rigidly restrained by grossly shortened chordae tendineae In other patients contraction of scar tissue in the valve cusps has so reduced their area that closure of the orifice would be impossible Such patients are not candidates for remedial surgery at present

Some degree of mitral stenosis is almost always present unless the rigid orifice is extremely capacious Extreme valvular incompetence does not coexist with serious stenosis According to Brock,[15] mitral insufficiency is a more advanced stage of valvular deformity than mitral stenosis Thus 'pure' rheumatic mitral insufficiency severe enough to have functional significance is probably a relatively rare lesion in which the heart functions as though there were no barrier between the left atrium and the left ventricle On a theoretical basis distinguishing between pure mitral stenosis and pure mitral insufficiency should be quite simple In practice this differentiation poses a most difficult diagnostic problem

Functional Effects of Advanced Mitral Incompetence

In advanced mitral incompetence filling of the ventricle is unimpeded but during systole blood is simultaneously ejected into the aorta and back into the left atrium The

ru h of blood back through the mitral orifice into the capacious atrial chamber produces turbulence perceived externally as a widely transmitted systolic murmur usually with maximal intensity in the apical region The blood tends to follow the course of least resistance o only a proportion of the total ejection enters the aorta Thus the stroke volume of the ventricle must be greatly increased to maintain arterial pressure and systemic blood flow Under such a sustained volume load the left ventricle should distend to much larger systolic and diastolic dimensions The quantity of blood entering and leaving the left atrial cavity is correspondingly increased so this chamber also labors under a volume load and should become dilated Contraction of the dilated atrium might be expected to expel an abnormally large quantity of blood increasing the terminal ventricular filling and also displacing a larger quantity of blood backward into the pulmonary veins Furthermore reflux of blood from the ventricle should exaggerate systolic expansion of the atrium which would be associated with a econd tall peak of pressure on the atrial pressure curve

Based on this analysis the *principal signs* of mitral incompetence should include (*a*) a loud systolic murmur in the mitral area (*b*) dilatation of the left ventricle (*c*) dilatation of the left atrium with augmented expansion during ventricular systole (*d*) exaggerated pulmonary venous pressure waves during both atrial and ventricular systole and (*e*) limited stroke volume and cardiac output reserve leading to fatigability These symptoms may be clearly manifested in an occasional patient with functionally pure mitral incompetence However most patients with mitral insufficiency also have some stenosis so the clinical picture becomes complicated

Apical Systolic Murmur Functional systolic murmurs can mimic those observed in patients with established mitral insufficiency Similar systolic murmurs are heard during initial attacks of rheumatic and nonspecific myocarditis and clearly do not indicate functionally significant mitral leakage They are not usually as loud as those commonly encountered with mitral regurgitation but their characteristics are similar Surprisingly enough not all patients in whom a retrograde jet is palpated by the exploring finger of the surgeon during cardiac surgery have detectable systolic murmurs For example Elkin et al[44] reported that 5 of 15 such patients had no systolic murmur Venner and Hollins[45] compared the clinical and surgical findings in 96 patients Nine patients had widely incompetent mitral valves and systolic murmurs but in one the intensity was no greater than that in persons with functional murmurs Thirteen of 61 patients without palpable regurgitation had loud apical systolic murmurs No distinguishing features between the systolic murmurs in patients with and in those without palpable regurgitation were noted From these observations systolic murmurs appear to be tenuous signs of mitral regurgitation and other evidence must be sought

Dilatation of the Left Ventricle In the absence of aortic valvular disease, roentgenographic evidence of gross left ventricular enlargement facilitates differentiation of mitral insufficiency and mitral stenosis In about half the patients with predominant mitral regurgitation the left ventricular contour is not remarkable on either roentgenograms or fluoroscopic examination Electrocardiograms provide evidence of left ventricular preponderance in about the same proportion and in the remainder right ventricular hypertrophy or combined ventricular hypertrophy may be indicated Since rheumatic carditis often affects more than one valve left ventricular enlargement can result from either mitral or aortic valvular disease Other causes for left ventricular enlargement such as heart failure hypertension and myocardial infarction must be kept in mind

Dilatation of the Left Atrium The atrium is dilated in a majority of patients with either mitral regurgitation or mitral

mitral regurgitation is particularly important in deciding the feasibility of mitral commissurotomy

MITRAL INCOMPETENCE

In the past, a diagnosis of mitral insufficiency was usually applied when an apical systolic murmur was too loud and persistent to be classified as "functional" Virtually all patients with acute rheumatic carditis develop systolic murmurs which persist for years With no additional confirmatory evidence, such patients were labeled as having mitral insufficiency Bland and Jones[34] reported the subsequent course of 87 patients with systolic murmurs on discharge from the hospital after their initial attack of rheumatic fever Twenty years later, 7 had mitral stenosis, 16 had mitral stenosis with evidence of regurgitation, 35 had mitral regurgitation diagnosed primarily on the presence of the murmur, and 29 no longer had the systolic murmur Clearly, the systolic murmurs so frequently discovered during initial attacks of acute rheumatic fever do not signify significant mitral incompetence Postmortem examinations on such patients are very rare and mitral incompetence cannot be reliably diagnosed by examining an excised heart unless the valvular deformity is severe In most patients, the changes in the valves following acute rheumatic valvulitis are believed to heal quite completely although the systolic murmur often persists On the basis of such evidence the significance of apical systolic mumurs in rheumatic patients deserves reappraisal

Types of Mitral Insufficiency

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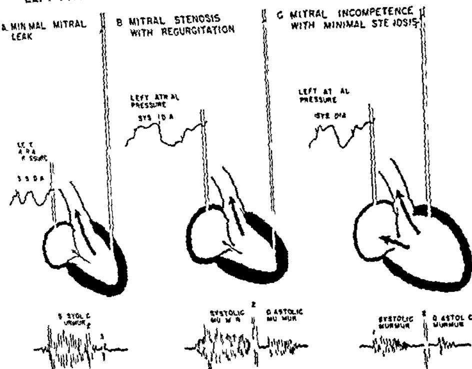


FIGURE 10 *A* If the mitral valves fail to seal completely during ventricular systole, a high velocity jet of blood regurgitates back into the atrium, *because of the large pressure difference* Such a regurgitant stream may produce very loud systolic murmurs *even though* the amount of blood regurgitating is functionally insignificant. The pressure fluctuations in the left atrium retain the normal configuration under these circumstances Since the circulatory load is minimal, the patient *may have* no symptoms or signs other than a loud systolic murmur maximally intense at the apex.

B Many patients with mitral stenosis have some degree of mitral insufficiency even though the regurgitation is not functionally significant Under these conditions, *the left atrium* tends to be enlarged, but the left ventricle remains small The intensity of the systolic and diastolic *murmurs* is not a reliable indicator of the relative severity of regurgitation and stenosis of the valve

C Free mitral regurgitation imposes a severe volume load on both the left atrium and the left ventricle which tend to become dilated Elevated left atrial pressure tends to diminish the pressure gradient producing the regurgitation. The flow through a large mitral defect could theoretically produce less turbulence than could the high velocity jet flowing through a very small orifice The left atrial pressure is elevated and the pressure waves *may indicate* the presence of mitral valvular disease although they reveal no characteristic differences between patients with predominant stenosis and patients with serious incompetence

nicely summed up by Burchell and Edwards[31] as follows The exposure by the surgeon of the physician's incompetence in diagnosing mitral incompetence (insufficiency) has in this era of mitral surgery been more acutely embarrassing to and less easily forgotten by the physician than the occasional errors of diagnosis previously pointed out by pathologists In the scramble to re-entrench themselves the internists have critically examined the traditional and new laboratory signs

PULMONARY VALVULAR INCOMPETENCE

The pulmonary valve is seldom affected by rheumatic valvulitis and even then the *functional* effects are usually insignificant The most common cause of pulmonary *valvular* incompetence is the dilatation of the pulmonary artery which usually accompanies pulmonary hypertension Patients with mitral stenosis *or* insufficiency characteristically have elevated pressures throughout the pulmonary vascular tree Pulmonary arterial

stenosis The force of a regurgitant jet of blood should exaggerate atrial expansion during ventricular systole The expansile pulsation of the left atrium produced by ventricular systole seen during fluoroscopy is frequently cited as evidence of mitral insufficiency When visualized, this sign is indeed highly suggestive of mitral insufficiency, but a word of caution seems warranted The equivalent of mitral regurgitation occurs during early systole in normal individuals During closure of the mitral valves, some blood probably leaks past the valve leaflets (see Chapter 13) As intraventricular pressure rises, the valves no doubt are displaced somewhat toward the atrium Supplemented by rapid atrial filling following atrial systole, the total effect should be a systolic expansion of the atrial chambers For these reasons, abnormal systolic atrial pulsation may be mistakenly reported On the other hand, it is frequently unrecognized in patients with mitral regurgitation confirmed by direct palpation Systolic pulsations are greatly damped by atrial distention because a very slight increase in circumference accommodates a relatively large volume Indeed, increased systolic distention of the left atrium may not be seen by direct observation of the atrium during surgical exploration [45] In spite of encouraging reports,[46] electrokymographic records are probably not greatly superior to fluoroscopic examination in eliciting this sign For example, Soloff et al [47] found that "plateau" curves, reported to be characteristic of left atrial border motion in organic mitral regurgitation, were obtained in 12 of 13 patients with an apical systolic murmur and also in 10 normal subjects

EXAGGERATED VENOUS PRESSURE WAVES A regurgitant jet of blood should produce a demonstrable increase in left atrial pressure which would facilitate diagnosis of mitral insufficiency Unfortunately, direct measurements do not consistently demonstrate an abnormal pressure pulse [45, 48] For example, Wynn et al [48] directly recorded pressures in 14 patients with normal hearts and in 37 patients before and after mitral valvulotomy In the 14 normal hearts, the atrial pressure rose 2 to 8 mm Hg during atrial systole and 1 to 9 mm Hg in late ventricular systole In 8 patients with mitral stenosis and evidence of mitral incompetence, the form of the pressure pulse was not significantly different (Fig 10) However, the amplitude of the pressure peaks was somewhat greater in 7 patients with mitral stenosis and with mitral regurgitation ranging from 3 to 19 mm Hg, in one patient the systolic peak reached 25 mm Hg

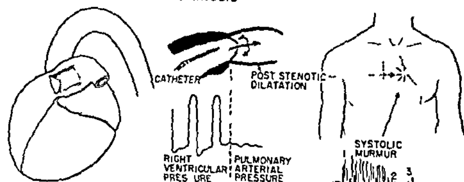
An attempt has been made to differentiate between mitral stenosis and regurgitation by recording the pressures from a catheter wedged in a terminal pulmonary artery Pressure contours diagnostic of mitral insufficiency were not found [49] The elevations of pulmonary artery and wedged catheter pressures and exaggerations of waves are similar in mitral stenosis and mitral regurgitation

RESTRICTED CARDIAC OUTPUT Draper et al [50] found that patients with both mitral stenosis and insufficiency had diminished cardiac output at rest In response to exercise, the cardiac output either increased or diminished slightly, the arteriovenous oxygen difference increased and a smaller proportion of oxygen was removed from the air exchanged in the lungs The high pulmonary arterial pressure at rest rose further during exertion They concluded that 'physiological methods alone do not permit a clear differentiation between mitral stenosis and mitral insufficiency' Certain characteristic differences were noted The resting cardiac output was lower and the arteriovenous oxygen difference was higher in patients with mitral regurgitation, who also more often displayed a reduction in cardiac output with exertion These observations are consistent with the principal complaint of such patients fatigue from very slight exertion

The extent to which current diagnostic methods fail to evaluate correctly the nature and degree of mitral valvular disease was

fundibular stenosis is a much more common cause of pulmonary obstruction in the tetralogy of Fallot (Chapter 19)

The mainstem of the pulmonary artery is often grossly dilated just beyond the valvular stenosis and even the right and left branches may be larger than normal in spite of diminished pulmonary blood flow This post-stenotic dilatation is a typical response to many kinds of local obstruction in the vascular system Holman[53] observed circumscribed dilatation in the arteries of dogs beyond experimental obstructions The post-stenotic dilatation was attributed to an increased lateral pressure from deceleration of the blood flowing at high velocity through a restricted orifice This explanation fails to take into account that the lateral pressure is



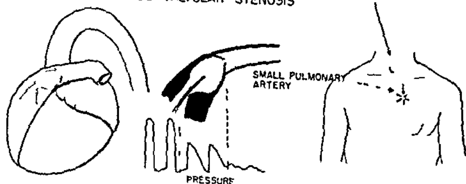


FIGURE 11 A Occasionally congenital stenosis of the pulmonary valve is an isolated lesion, but it is usually accompanied by defects in either the *atrial* or the ventricular septum (see Chapter 19) The pulmonary valve consists of a conical diaphragm *with a small* aperture at the apex and the pulmonary artery beyond the valve is usually dilated (post-stenotic dilatation) *To overcome* the high resistance to flow through the restricted valvular orifice the right ventricular systolic pressure becomes greatly elevated. The mean pulmonary arterial pressure beyond the *constriction* is normal or diminished but the *pulse* pressure is greatly reduced Turbulent flow of blood through *the small* orifice produces a systolic *murmur which* is widely transmitted over the precordium but has maximal *intensity* in the pulmonary area Post-stenotic *dilatation* of the pulmonary artery produces a prominent bulge on the left border of the mediastinal shadows in the postero-anterior position Right ventricular hypertrophy is more easily detected with the *patient* in the left anterior oblique position (see drawing on the left)

B A combination of infundibular and *valvular* stenosis produces signs *and* symptoms similar to those of isolated pulmonary valvular stenosis In this condition, the pulmonary artery is generally hypoplastic rather than dilated Pressure records obtained *during slow* withdrawal of a catheter usually demonstrate a stepwise change in pressure rather than the abrupt change in pressure *patterns* observed with isolated pulmonary valvular stenosis (After Kirklin, J W et al 32)

hypertension is greatly increased by pathologic changes in the lungs or by sclerosis in the terminal pulmonary arterial branches, as illustrated in Figure 8. Such pulmonary *sclerosis is also caused by* various congenital malformations of the heart which greatly increase pulmonary blood flow, including interatrial septal defects, patent ductus arteriosus and the Eisenmenger complex (see Chapter 19). Dilatation of the mainstem pulmonary artery may become sufficiently severe under these circumstances *to induce widening* of commissures between the pulmonary valve cusps and cause pulmonary valvular incompetence. The functional disturbances following dilatation of the pulmonary artery with commissural widening between the cusps correspond to those following syphilitic aortic insufficiency. The actual magnitude of the regurgitation is *usually small even though the diastolic murmur* may be prominent. The pulmonary arterial pressures are elevated. The right ventricle is generally hypertrophied by the antecedent pulmonary hypertension and assumes some of the functional and anatomic characteristics of the left ventricle (thick wall and rounded chamber). Since murmurs from *pulmonary and aortic valvular abnormalities* may both have maximum intensity in the third intercostal space to the left of the *sternum murmurs caused by pulmonary in*sufficiency cannot always be distinguished from those associated with aortic insufficiency or aortic stenosis with insufficiency. This is unfortunate, since they have very different significance. If pulmonary incompetence is mistaken for aortic insufficiency, a patient with stenosis of the *mitral or aortic valves may* be denied corrective surgery. The left ventricle should be greatly enlarged by aortic insufficiency while the right ventricle is *generally* enlarged by pulmonary hypertension. The uncertainties of roentgenographic diagnosis are such that this distinction is not as clear-cut as it might seem (see Chapter 11). Ordinarily a dilated pulmonary artery can be clearly visualized as a prominent bulge on the left border of the mediastinum (see Fig 14, Chapter 11). *Such a shadow should be* considered carefully in evaluating the significance of systolic and diastolic murmurs heard at the base of the heart.

There is no need to dwell upon this condition beyond reiterating that its principal significance lies in identifying the cause of systolic and diastolic murmurs with *maximum intensity at the base of the heart*. *Since* pulmonary insufficiency frequently develops as a complication of pulmonary hypertension from other cardiac or pulmonary disease, an uncomplicated picture of simple pulmonary valvular incompetence is rarely encountered. The therapy consists of taking whatever measures are available to alleviate pulmonary hypertension.

PULMONARY VALVULAR STENOSIS

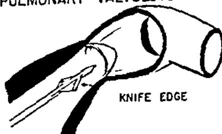
Stenosis of the pulmonary valve is a rare condition, and most examples are found among patients with congenital malformations of the heart. Developmental defects in which pulmonary stenosis is associated with apertures in the septa of the heart are considered in Chapter 19. Congenital isolated *pulmonary stenosis is* considered briefly here among the chronic valvular diseases even though stenosis of this valve is com*monly accompanied by a defect in the inter*atrial septum.

Three main types of congenital pulmonary stenosis are found: valvular stenosis, infundibular stenosis and a combination of the two[54] (Fig 11). In the first type, the pulmonary valvular cusps are fused during embryologic development into a diaphragm *or conical membrane* with a small central orifice. Infundibular stenosis sometimes develops as a long narrow muscular channel replacing the *normally capacious* outflow tract of the right ventricle. More commonly, there is a narrow constriction at some level below the pulmonary valve. As an isolated lesion, valvular stenosis is much more common than infundibular stenosis; occasionally they occur together. In contrast, in-

sharp drop in pressure in the pulmonary artery (Fig 11) The constriction in the outflow tract of the right ventricle can often be demonstrated by angiocardiography particularly with the patient in the right anterior oblique position

Treatment of Pulmonary Stenosis

Surgical alleviation of the infundibular or valvular obstruction is warranted whenever symptoms have developed in a patient with a definitive diagnosis of pulmonary stenosis Remedial surgery is recommended if cardiac catheterization demonstrates right ventricular systolic pressures in excess of 75 mm Hg even if symptoms have not developed because the prognosis is unfavorable without therapy [52,35] Congenital valvular stenosis occurs so early in cardiac development that commissures are not well delineated For this reason valve dilators produce indiscriminate tears which alleviate the stenosis but may produce serious incompetence Instead a linear incision directly across the valve is produced to form a functionally bicuspid valve (Fig 12*A*) Therapy of infundibular stenosis has been a most difficult problem Dilatation has not proved of lasting worth Brock[55] has developed a technique by which the muscular tissue obstructing the right ventricular outflow tract is excised piecemeal until an adequate caliber is attained (Fig 12*B*) His favorable results obtained with this procedure have not been duplicated in this country Recently hypothermia during surgery has been used to provide an opportunity for correcting the pulmonary stenosis under direct vision by incising the pulmonary artery If the body temperature of the patient is diminished sufficiently under carefully controlled conditions the metabolism is so slowed that the circulation can be completely arrested long enough to perform intracardiac surgery [57] The development of mechanical heart lung apparatus is being intensively pursued in many laboratories When such equipment is perfected the horizons of cardiac surgery will be greatly expanded because intracardiac defects can be repaired under direct vision in bloodless hearts



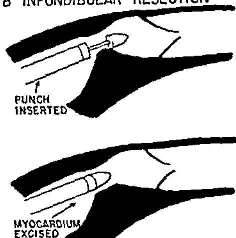


FIGURE 12. *A* Pulmonary valvular stenosis can be alleviated surgically by a transverse incision across the abnormal valve by means of a valvulotome *B* The constricting ring of myocardium producing infundibular stenosis may be resected piecemeal The technique illustrated above was devised by Brock.[55]

TRICUSPID STENOSIS

The most common cause of tricuspid stenosis is rheumatic valvulitis The incidence of tricuspid deformity associated with other valvular lesions is greater than is generally recognized For example O Neill et al [58] reviewed the literature and found that of 806 patients with valvular disease 90 per cent had lesions in the mitral valve and 30 per cent had tricuspid deformities The fact that mitral and tricuspid disease without other valvular involvement occurred in

higher above the obstruction than beyond it Turbulence beyond such an obstruction throws the walls into vibration and may induce structural fatigue

Functional Effects of Pulmonary Stenosis

Constriction of the outflow tract of the right ventricle imposes a requirement for a greater systolic ventricular pressure to eject the normal complement of blood into the pulmonary artery Obviously, the magnitude of the pressure gradient between the right ventricle and the pulmonary artery depends upon the resistance to outflow (caliber of channel) and the velocity of blood flow The basic problem is the same as that presented by aortic stenosis In a case of infundibular stenosis, cinefluorographic angiocardiograms indicated that the caliber of the narrowed channel was greatly diminished during systole, apparently by constriction of the surrounding myocardium Such constriction serves to augment impedance to right ventricular outflow during systolic ejection The systolic pressure in the right ventricle ranges from high normal values to levels exceeding 200 mm Hg [52] The normal right ventricle is ill prepared to develop such high intraventricular pressure As has been repeatedly mentioned, a long-continued right ventricular pressure load causes the right ventricle to assume many of the characteristics of the left ventricle This is particularly true in congenital malformations where the load is present at least from birth The right ventricular wall is very thick (often exceeding 1 cm) The chamber is more rounded in contour instead of having a crescentic cross section So long as myocardial hypertrophy is an adequate compensatory mechanism, right ventricular dilatation is not functionally significant The rush of blood through the constricted pulmonary outflow tract produces intense turbulence, with loud systolic murmurs occupying most of the systolic interval but often exhibiting maximal intensity in mid-systole (such as occurs with aortic stenosis)

Symptoms of Pulmonary Stenosis

Many patients with isolated pulmonary stenosis have no symptoms whatever Their growth, appearance, exercise tolerance and subjective feeling of well-being are deceptively normal When the condition is more severe, mild or moderate dyspnea on exertion and occasional palpitation are noted, even when the right ventricular systolic pressure is as high as 170 mm Hg [54] If the orifice is small, the principal effect is limitation in the maximum cardiac output which can be maintained by the right ventricle From the graph in Figure 7 it is clear that very high pressures may be required to provide high-velocity flow through restricted apertures Right ventricular failure is the principal hazard in these patients

Diagnostic Signs of Isolated Pulmonary Stenosis

The murmur of pulmonary stenosis is widely transmitted over the precordium, but usually is loudest in the pulmonary area, the third intercostal space at the left sternal margin It is important to recall that the murmur of aortic stenosis may also have maximal intensity in that area in some patients Evidence of right ventricular hypertrophy is best observed roentgenographically in the left anterior oblique position Electrocardiograms usually provide confirmatory evidence of right ventricular preponderance (e g , Fig 22, Chapter 15) Valvular stenosis with post-stenotic dilatation usually can be identified in the anteroposterior position by the local bulge on the left of the mediastinum in the presence of diminished vascular markings in the lung fields (Fig 11) In patients with infundibular stenosis, the mid-portion of the left border of the cardiac silhouette is normal or concave (see also Chapter 19) Fluoroscopic examination is useful for demonstrating diminished pulsations of the pulmonary vessels

During cardiac catheterization, a definitive diagnosis of pulmonary stenosis can be obtained if systolic pressures in the right ventricle are elevated and accompanied by a

the functioning heart Since accurate preoperative diagnosis is exceedingly important in planning an optimal approach the discovery of major or minor errors in diagnosis in 15 to 50 per cent of patients has prompted a re-examination of all possible diagnostic criteria

Most disappointing of all has been the inconstancy of murmurs in the various valvular lesions Murmurs may be completely absent or misleading in any of the different types of valvular deformities It is now clear that all possible sources of information must be carefully evaluated to reach a judgment concerning the site and nature of valvular deformities This situation results from two different factors (a) rheumatic fever the most common cause of valvular disease usually affects more than one valve and (b) individual valvular lesions are often difficult to differentiate from each other For example, mitral stenosis is very often complicated by mitral insufficiency and the presence or degree of regurgitation cannot be accurately assessed even using every available technique including cardiac catheterization Furthermore the murmurs of mitral stenosis are easily confused with similar murmurs associated with aortic insufficiency and tricuspid stenosis At the present time the only diagnosis which can be unquestionably established by a direct measurement is pulmonary stenosis A marked pressure drop between the right ventricle and the pulmonary artery recorded during cardiac catheterization demonstrates a constriction in the outflow tract of the right ventricle due to either valvular or infundibular stenosis In some patients a distinction between these two types of pulmonary stenosis can be made Techniques for inserting needles and tubes into the left atrium promise improved accuracy in diagnosing defects in the mitral and aortic valves if they become established as practical and safe

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about 7 per cent of patients was considered important because of the similarity in the clinical signs of the two conditions The diagnosis of tricuspid stenosis is rendered very difficult by the presence of mitral valvular disease, and may become evident only after mitral commissurotomy is followed by limited improvement in the patient's condition Since the right atrium is not readily accessible through the surgical exposure used for mitral commissurotomy, lesions of the tricuspid valve cannot be detected and treated during routine operations on the mitral valve For this reason, signs of functionally significant tricuspid valvular deformities should be ruled out as completely as possible preoperatively

Functional Effects of Tricuspid Stenosis

A restricted tricuspid orifice impedes blood flow into the right ventricle and is compensated by elevated pressures in the right atrium and systemic veins Thus, tricuspid stenosis produces elevated venous pressure and venous congestion upstream, but for reasons unknown, the splanchnic bed and liver are most seriously affected Thus ascites is more prominent than peripheral edema in patients with tricuspid valvular disease The right atrium tends to become enlarged and hypertrophied The powerful right atrial contraction produces very large atrial pressure waves which can often be directly observed in the jugular veins

Diagnostic Signs of Tricuspid Stenosis

Patients with evidence of chronic valvular heart disease developing transient or constant ascites and peripheral edema with little or no sign of pulmonary congestion (e g dyspnea) should be carefully examined for tricuspid stenosis The murmurs produced by mitral and tricuspid stenosis differ only in their distribution over the precordium The diastolic murmurs of tricuspid stenosis tend to localize over the xiphoid process and toward the right of the lower sternum However, the diagnosis is rarely made on the murmur alone A vigorous pulsation of the jugular veins may be demonstrated as presystolic by palpating the carotid artery on the opposite side Catheterization of the right atrium generally demonstrates the "giant" A wave, but since this occurs with pulmonary stenosis and tricuspid insufficiency as well, further exploration is required A definite pressure drop between the right atrium and right ventricle is the most direct evidence of tricuspid stenosis The therapy for this condition consists of commissurotomy just as in mitral stenosis

TRICUSPID INSUFFICIENCY

Rheumatic tricuspid valvulitis is rarely severe enough to cause functionally significant incompetence and regurgitation Thus, tricuspid insufficiency is generally the result of extensive right ventricular dilatation with expansion of the valve ring Incompetence of the tricuspid valve is generally due to extensive disease in the heart and lungs, the signs or symptoms of which tend to overshadow the tricuspid lesion It is often difficult to differentiate tricuspid insufficiency from tricuspid stenosis because they both accompany other cardiac disease states Also, they both produce enlargement of the right atrium, increased atrial pressure waves increased pressure and congestion in systemic veins and ascites It may be possible to distinguish the two conditions on the basis of differences in the venous pulse[59] but this is not absolutely reliable

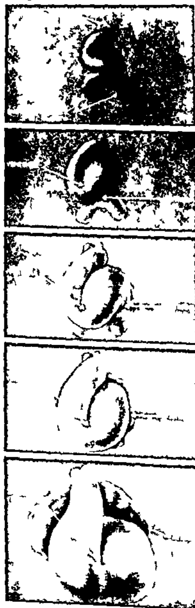
SUMMARY

In the past a great deal of reliance has been placed on the character timing and localization of murmurs to identify stenosis and insufficiency of the individual cardiac valves Since the diagnosis generally could not be checked until a postmortem examination was performed, this method of valvular diagnosis was considered accurate The advent of cardiac surgery has provided an opportunity to evaluate the diagnostic signs in

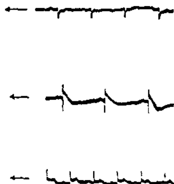
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A THE CONVOLUTED CARDIAC TUBE



B ELECTRICAL ACTIVITY



C PRIMITIVE VALVE FUNCTION





FIGURE 1 *A* The initial stage in the development of the heart is the formation of a single cardiac tube which will ultimately evolve into the ventricular portion of the heart. At this very early stage contractions occur repetitively at a slow rate. Being anchored above by the developing arterial trunks and below by extensive venous channels the cardiac tube, growing rapidly in length is bent into a loop to the right of the midline By progressive fusion of the cardiac primordia the primitive atrium is formed, and remains relatively fixed in position as the cardiac loop grows longer and swings back to the midline to cover the expanding atrial chambers In this process the ventricle assumes a position anterior and caudal to the atria.

B Electrical activity can be recorded from the heart of the chick embryo at the very early stages of development, indicated by the first three drawings in Figure 1*A* As the cardiac tube becomes convoluted the electrocardiographic patterns produced by this electrical activity begin to resemble the patterns observed in fully developed hearts (After Hoff et al.[3])

C Contraction of the cardiac tube is peristaltic in character beginning in the atrial region and progressing toward the truncus arteriosus During contraction at the atrioventricular junction the endocardial surfaces come into apposition to prevent retrograde flow of blood. A similar valve action may be observed at the root of the truncus arteriosus (After Patten et al.[4])

Chapter 19

Congenital Malformations of the Heart

Malformation of the heart during embryologic development was primarily of academic interest so long as no specific therapy was available During the past 15 years, surgical techniques have been devised to alleviate or eliminate certain congenital defects The consequent necessity for distinguishing cases suitable for surgical therapy has resulted in a widespread effort to develop and improve the techniques for differential diagnosis of all these conditions The origin and nature of the various types of developmental defects can best be visualized as aberrations of normal embryologic processes For this reason, the salient features of the normal development of the heart are presented Much of the illustrative material in this chapter has been derived from a series of motion picture films[1] dealing with the origin, functional effects and diagnostic signs of congenital malformations of the heart

THE DEVELOPMENT OF THE NORMAL HEART

During embryologic development, the various tissues and organs rapidly pass through stages representing the evolutionary development of the species For this reason, the extensive investigation of embryology in the chick is generally applicable to human embryos, but there is one important difference the chick embryo develops on the surface of an abundant yolk

The heart develops from a pair of primordial tubes derived from clusters of endothelial cells which proliferate and become organized into strands of cells and acquire a lumen The paired endocardial primordia are located near the margin of the anterior intestinal portal and are brought closer together by the infolding process which produces the foregut These primitive tubes meet in the midline and fuse into a single elongated chamber which will ultimately develop into the ventricles From the simple cardiac tube, the endocardial primordia proliferate toward the head to form the aortic arch system The caudal extensions of the primordial tubes become the omphalomesenteric veins As the formation of gut proceeds caudally, fusion of the primordial tubes continues, forming the primitive atrium and finally the sinus venosus

Convolution of the Cardiac Tube

The primitive cardiac tube grows longer more rapidly than either the investing pericardium or the surrounding somatic structures It is anchored above by the arterial trunks and below by developing venous channels Since the tube is fixed at both ends, its rapid elongation causes flexion, initially toward the right side of the embryo As elongation continues, the cardiac tube becomes more tortuous (Fig 1*A*) At the same time, constrictions develop which indicate the ultimate division of this single convoluted tube into atria and ventricles As the ventricular region progressively expands and grows longer, it swings back toward the midline to cover the atrial region which remains relatively fixed in position In this process the primitive atrium and arterial trunks, which were originally on opposite ends of the cardiac tube, are brought into ap-

cardial tissue later fuse to form a column which splits the stream of blood flowing from atrium to ventricle (Fig 2C) At the same time a muscular septum proliferates from the interventricular groove toward the base of the heart separating the right and left ventricles

In the atrium a crescentic ridge (septum primum) appears on the dorsocephalic part of the atrium and rapidly grows down toward the ventricle As this septum grows across the common atrial chamber the aperture between the right and left atria (foramen primum) is progressively constricted (Fig 2D) However before the foramen primum is completely closed a new opening (foramen secundum) appears high on septum primum (Fig 2E) The timely development of the foramen secundum prevents interruption in the shunting of blood from the right atrium into the left

Another septum (secundum) develops just to the right of the septum primum and extends like a curtain down over the aperture in the septum primum (Fig 2F) The septum secundum grows beside the septum primum to become a second atrial partition which is complete except for a persistent aperture

PARTITIONING OF THE HEART

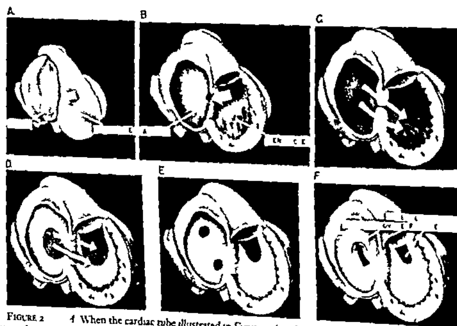


FIGURE 2 A When the cardiac tube illustrated in Figure 1 A is observed in a lateral view the atrium and ventricles appear to be divided by a deep atrioventricular invagination.
B Actually this groove is merely a constriction at the atrioventricular junction The embryonic heart at this stage is still a simple tube which has become convoluted and expanded into primitive chambers A four chambered heart with corresponding arterial trunks is formed by the elaboration of three septa dividing the atria ventricles and truncus ateriosus
C First, the atrioventricular channel is divided at its waist by proliferating endocardial cushions which fuse into a column
D Septa dividing the atrium and ventricle grow simultaneously toward the atrioventricular grooves If either of these partitions fails to form, the fully developed heart has only a single atrium or a single ventricle
E An aperture in the developing atrial septum persists near its junction with the endocardial cushions (the foramen primum) Before foramen primum is closed, a new aperture appears high on the interventricular septum (foramen secundum) These two embryonic apertures are the most common sites of interatrial septal defects
F The foramen secundum is covered by the developing septum secundum which grows down over the aperture Its advancing edge becomes thickened to produce the foramen ovale which acts as a unidirectional flutter valve Closure of the interventricular foramen awaits the development of a complex spiral septum dividing the truncus arteriosus and conus region of the primitive ventricle (see Fig 3)

position Thus, the inflow tract and outflow tract are adjacent and all four valve rings ultimately merge into a single fibrous skeleton (see Fig 1, Chapter 1) The developing atria expand laterally to form two extensive sacculations, the primitive right and left atria These sacculations ultimately become the right and left auricles, while the main atrial chambers develop by progressive incorporation of the venous channels into the posterior wall

The Initial Cardiac Contraction

According to Patten,[2] the first signs of contraction of the heart in chick embryos appear while the heart is represented by only the ventricular portion of the cardiac tube (Fig 1) Localized slow contractions are usually noted first on the right margin near the root of the primitive arterial trunks However, the site and spread of these earliest undulations vary considerably The initial contractions in the embryonic rat heart occur a few hours before the elaboration of fibrillae or cross striations[3] About an hour after the first fibrillar contraction appears, the entire primitive ventricle contracts regularly and synchronously, but at a slow rate The character of the contraction changes a few hours later as the atrium is formed At this time, contractions originate in the atrial region and sweep over the ventricle like a peristaltic wave The atrium assumes the role of pacemaker because of its higher inherent rate of impulse formation (see Chapter 14) The sinus venosus has an even faster inherent rhythm and assumes control as soon as it is formed The sinus venosus ultimately forms the sinoatrial node, the normal pacemaker of the fully developed heart

By the time the atrium and sinus venosus are formed, this primitive tubular heart is actively pumping blood through the developing circulatory system During the peristaltic type of cardiac contraction retrograde flow of blood is prevented by developing mounds of endocardial tissue which project into the lumen at the junction of the primitive atria and ventricles[4] During each contraction these endocardial cushions make contact, completely blocking the channel (Fig 1*C*) Thus, simple but effective atrioventricular valves are formed at this very early stage of development Similar endocardial cushions develop in the outflow tract near the ventricular conus This region ultimately develops into the conus of the right ventricle

The Development of the Electrocardiogram

According to Hoff et al,[5] electrical activity can be consistently recorded from chick embryos at the stage of development illustrated in Figure 1*A* A few hours later there is a sharp downward deflection which is interpreted as equivalent to a QRS complex In the next three or four hours the atrium has become differentiated and the sinus venosus appears At about this time, downward deflections (P waves) can be recorded just preceding the QRS As the primitive cardiac tube becomes convoluted, the electrocardiogram assumes a configuration similar to that of the adult (Fig 1*B*)

Partitioning of the Atrioventricular Canal

At six weeks of age, the major components of the human heart can be readily identified (Fig 1*A*) A shallow, interventricular groove forms a line of demarkation between the future right and left ventricles

In spite of the apparent separation of the atria from the ventricles at the atrioventricular junction (Fig 2*A*, arrow) the heart actually consists of a common atrioventricular canal which empties into a single arterial trunk A four-chambered heart is developed from this convoluted, dilated tube by the formation of three partitions separating the atria, the ventricles and the two main arteries

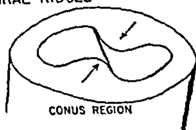
The first step in division of the atrial and ventricular chambers begins with the proliferation of endocardial cushions from the dorsal and ventral portions of the atrioventricular groove These masses of endo-

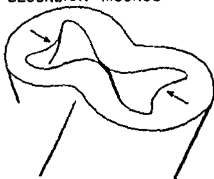
conus region just above the partially divided ventricular chambers to its bifurcation into the aorta and pulmonary arteries A pair of ridges appearing at the bifurcation and on opposite sides of the truncus arteriosus pursue a spiral course toward the ventricles (Fig 3B) These ridges grow toward the axis of the cylinder and fuse to form a continuous spiral septum which twists 180 degrees and swings into line with the advancing edge of the interventricular septum (Fig 3C) The spiral form of the aortic pulmonary septum accounts for the manner in which the pulmonary artery and aorta intertwine in the fully developed heart (Fig 3E)

The remaining interventricular foramen is closed by proliferating endocardial tissue from the atrioventricular cushions the interventricular septum and the spiral aortic pulmonary septum (Fig 3D) The connective tissue which occludes the interventricular foramen gradually thins out to form the membranous portion of the interventricular septum

The Formation of Cardiac Valves

The semilunar valves begin to form during the division of the truncus arteriosus into the aorta and pulmonary artery (Fig 4A) At the junction of the ventricular conus and the truncus arteriosus the spiral ridges on opposite sides of the channel develop localized pads of embryonic connective tissue (Fig 4B) As the spiral ridges grow across the lumen these endocardial cushions form two projections into each vessel and a third pad of tissue grows into each vessel from a point opposite the line of fusion of the spiral septum (Fig 4B) In this way three pads of connective tissue project into the lumens of the vessels and are gradually excavated and molded into valve cusps forming semilunar valves (Fig 4C) The formation of the atrioventricular valves cannot be so readily visualized Thick flaps of tissue proliferate from the region of the atrioventricular junction down into the ventricular chamber The exact mechanism by which these crude flaps are converted into beautifully formed valve cusps intricately guyed by chordae





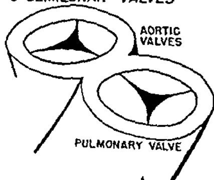


FIGURE 4 *A* The semilunar valves develop during the separation of the truncus arteriosus by the spiral aortic pulmonary septum (see Fig 3)

B Pads of endocardial tissue develop at the site of the valves. These pads originate from the spiral aortic pulmonary septum and as secondary mounds on opposite sides of the channel.

C When partitioning of the truncus arteriosus is complete three pads of endocardial tissue appear in the aorta and in the pulmonary artery These pads are shaped and thinned out to produce the semilunar aortic and pulmonary valves

PARTITIONING OF THE ARTERIAL TRUNKS

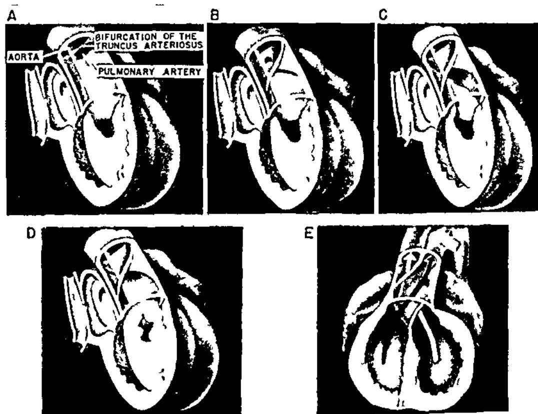


FIGURE 3 *A* The truncus arteriosus is illustrated as a transparent cylinder with the heart viewed in the right anterior oblique position

B, A pair of spiral ridges develop in the internal surface of the truncus arteriosus beginning at the bifurcation of the truncus arteriosus into the fourth and sixth aortic arches Retaining their positions on opposite sides of the cylinder the ridges pursue a spiral course toward the ventricles

C, The ridges grow into the lumen and fuse to produce a spiral septum which extends into the conus region of the ventricles where they swing into line with the upper margin of the interventricular septum.

D, The interventricular foramen is normally obliterated by masses of endocardial tissue growing from the ventricular septum the endocardial cushions and the spiral aortic pulmonary septum This mass of endocardial tissue thins out to form the membranous portion of the interventricular septum just below the origin of the aorta and pulmonary artery This is the most common site of interventricular septal defects

E The significance of the spiral aortic septum is more readily appreciated in a frontal view of the heart The aortic pulmonary septum executes a spiral of about 180 degrees and swings into line with the superior margin of the interventricular septum This process accounts for the manner in which the aortic and pulmonary trunks are entwined in the fully developed heart Blood from the left ventricle enters the aorta which passes to the right behind the pulmonary artery The pulmonary artery passes in front of the aorta and turns posteriorly on the left side of the mediastinum

adjacent to the foramen secundum The thickened edge of this aperture forms the margin of the foramen ovale Thus are formed two parallel partitions having apertures which are adjacent but not superimposed The septum secundum eventually becomes fused to the septum primum except at the foramen ovale Here the thin septum primum acts as a unidirectional flutter valve, permitting blood to flow only from the right atrium into the left Blood cannot flow in the opposite direction because pressure in that direction presses the valvula (septum primum) against the orifice The functional significance of this unidirectional valve is considered below in relation to circulatory adjustments after birth Closure of the interventricular foramen awaits the partitioning of the conus and truncus arteriosus

The Spiral Aortic Pulmonary Septum

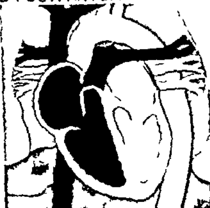
The truncus arteriosus resembles a cylinder (Fig 3*A*), extending from the

CIRCULATORY ADJUSTMENTS AT BIRTH

A FETAL PATTERN



B POSTPARTUM



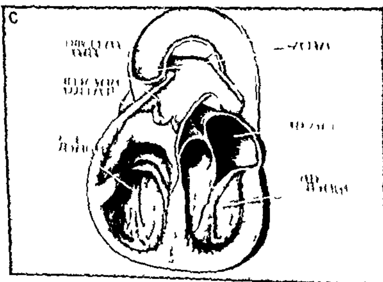


FIGURE 6 *A* The fetal circulatory pattern is adapted for intra-uterine existence Venous blood from the superior vena cava flows into the right atrium and *predominantly into* the right ventricle This unsaturated blood is ejected into the pulmonary artery where a *major* portion continues through the ductus arteriosus into the descending aorta Resistance to flow *through the collapsed lung* is so great that only a small quantity of blood enters the pulmonary arteries A correspondingly *small amount of blood* returns to the left atrium through the pulmonary veins Oxygenated blood from the placenta joins the blood flowing through the inferior vena cava and tends to stream across the right *atrium* through the foramen ovale into the left atrium This flow of oxygenated blood into the left atrium supplements the scanty venous return from the lungs The mixture of oxygenated and unsaturated blood enters the *left ventricle* and is pumped into the aorta from which the carotid arteries arise to supply the brain In the *descending* aorta, this blood is joined by unsaturated blood flowing through the ductus and the mixture is distributed to the lower portions of the body

B Very shortly after birth the flow of *oxygenated blood* from the placenta is interrupted Respiratory function of the lungs must be promptly initiated if the infant is to survive Pulmonary expansion greatly diminishes pulmonary resistance and the pulmonary blood flow is *greatly increased* Constriction of the ductus arteriosus diverts the entire right ventricular outflow into the pulmonary circuit When the increased pulmonary flow elevates left atrial pressure sufficiently to close the *foramen ovale* the adaptation to extra-uterine *existence is* complete

C The components of the fully developed heart are illustrated as viewed from the left anterior oblique position for comparison with drawings portraying various developmental *defects*

tendineae arising from the appropriate papillary muscles, is not clear

The Ductus Arteriosus

Both the pulmonary arteries and the ductus arteriosus are *remnants of the sixth* pair of aortic arches Like all the other pairs of aortic arches *the sixth connects the* ventral and the dorsal aorta and corresponds to the gill arches in fishes *Branching* vessels arise from both the right and left limbs of the sixth aortic arch to supply the *developing* lungs As the pulmonary branches from the right aortic arch develop, communication with the dorsal aorta regresses and ultimately disappears The remnant of the sixth aortic arch between the pulmonary artery and the left aortic arch persists as the ductus arteriosus (Fig 5) During fetal life, blood ejected by the right ventricle can bypass the pulmonary circuit and enter the descending aorta The functional significance of this short circuit is more clearly visualized in relation to the fetal circulation as a whole

THE ORIGIN OF THE DUCTUS ARTERIOSUS

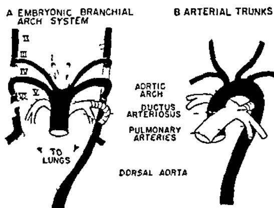


FIGURE 5 *A* The major arterial trunks originate by expansion and resorption of the various portions of the embryonic branchial arch system The aortic arch develops from the left branch of arch IV and right arch IV ultimately continues as the right subclavian artery The pulmonary arteries to the right lung develop from right arch VI and the right dorsal aorta normally disappears

B The connection between arch VI and the aorta on the left persists as the ductus arteriosus The main *pulmonary artery* is divided from the ascending aorta by the spiral aortic pulmonary septum as indicated in Figure 3

CIRCULATORY CHANGES AT BIRTH

The early embryologic development of the circulatory system is characterized by the formation and regression of various channels to accommodate the growth patterns of the developing structures By the eleventh week, the heart of a human embryo has been formed into a four-chambered heart with the corresponding arterial trunks The circulatory pattern established at this time persists throughout the remainder of fetal development

The Fetal Circulation

While the fetus remains in the uterus, the basic functions of respiration, digestion and elimination of waste products are carried out by the mother The circulatory system must perform its logistic function during this parasitic type of existence and yet be capable of rapid accommodation to independent existence immediately *after the fetus is delivered* to the external world Since the most critical commodity in both *the fetus and the* newborn infant is oxygen, the mechanisms required *for independent respiratory activity* have great importance

In the fetus, the lungs are collapsed and have no respiratory function The resistance *to the flow of blood through* the vessels of atelectatic lung tissue is extremely great Before birth, the vascular resistance is so much greater in the pulmonary vasculature than in the systemic circulation that most of the flow is diverted around the lungs The foramen ovale and ductus arteriosus act as bypasses permitting blood from the systemic veins to enter the systemic circulation without passing through the lungs

If there were no orifice in the interatrial septum left ventricular output would be restricted to the quantity of blood flowing through the lungs Under these conditions the left ventricle pumps abnormally small amounts and may not *develop normally* For example Patten[6] illustrated the heart from *an infant in whom the foramen* ovale was sealed prematurely, the left ventricular

tion of smooth muscle within its walls [12] Barclay et al [13] reported angiocardiographic studies indicating that the ductus arteriosus is functionally closed 5 or 7 minutes after respiration begins although the contrast medium was observed to flow through the channel intermittently for a considerable period However Everett and Johnson [14] employing sensitive radioisotope techniques found some reduction in ductus arteriosus flow 1 to ~ hours after birth but a greater reduction after 9 hours A small slitlike lumen in the ductus persisted from about the twelfth hour post partum until the eighteenth day when anatomic obliteration was usually complete Eldridge et al [15] demonstrated that the oxygen content of arterialized blood from the hand and from the feet are different immediately after delivery This difference persisted during observations lasting 3 hours and was still observable in some infants after 3 days The lower oxygen content of blood from the feet was attributed to shunting of venous blood through the ductus arteriosus into the aorta The oxygen content of arterialized blood in the upper and lower extremities apparently becomes equal when the ductus arteriosus is closed or the direction of flow through this channel has reversed because pressure in the pulmonary artery was lower than that in the aorta

It is entirely possible that functional closure of the ductus arteriosus in human infants requires a period longer than the times observed during controlled experiments in animals Hamilton et al [16] stated that the ductus arteriosus in both dog and rabbit contains valvelike structures which prevent flow from the aorta into the pulmonary artery This conclusion is not universally accepted Similarly reports concerning the time required to complete anatomic obliteration of the channel vary widely According to Scammon and Norris [17] the ductus arteriosus is obliterated by connective tissue proliferation during the first three months after delivery The persistent patency of the ductus arteriosus in a small proportion of patients is one of the simplest form of congenital heart disease and will be considered in a subsequent section

Closure of the Foramen Ovale. Soon after birth, the blood flow through the pulmonary circuit increases greatly because of the reduced resistance which follows inflation of the lungs Functional closure of the ductus arteriosus diverts the entire right ventricular output through the lungs These factors greatly increase the pulmonary venous flow into the left atrium As soon as the left atrial pressure exceeds right atrial pressure the valvula is pressed against the margin of the foramen ovale and partitioning of the heart is finally complete Anatomic obliteration of the potential aperture of the foramen ovale requires many weeks or years In fact about 20 per cent af all adults have at least probe patency of this orifice [18] a phenomenon without functional significance unless pressure in the right atrium subsequently becomes higher than that in the left Under these conditions the interatrial communication will be restored and may even enlarge until significant quantities of venous blood are shunted into the left atrium

Changes in Arterial Pressure after Birth The pulmonary arterial pressure immediately before birth probably ranges around 60/40 mm Hg and slightly exceeds systemic arterial pressure As pulmonary resistance falls and systemic arterial resistance rises the pressures in the pulmonary artery and aorta diverge progressively Ultimately they reach the values typical of adults systemic arterial pressures 120/80 and pulmonary arterial pressure 25/8 By this time the pressures in the left atrium left ventricle and aorta exceed the corresponding pressures on the right side of the heart Judging from certain clinical observations the systemic and pulmonary pressures diverge slowly in the human infant For example many infants with defective partitions in the heart or great vessels have no audible murmurs at birth and for weeks or months thereafter The

cavity was very small and the wall was poorly developed The fetal circulatory pattern can be viewed in terms of the mechanisms by which the output of the two ventricles can remain comparable in the face of greatly retarded pulmonary flow (Fig 6A)

The flow of blood through the circulatory systems of human fetuses delivered by legal abortion has been studied angiocardiographically by Lind and Wegelius [7] Blood returning from the placenta flows through the umbilical vein and enters the ductus venosus and vascular networks of the liver This blood carries oxygen and nutrient materials delivered by the maternal blood in the placenta Entering the vena cava, this partially oxygenated blood merges with systemic venous blood from the caudal portions of the fetus Much of the blood flowing from the inferior vena cava into the right atrium streams across the chamber and passes through the foramen ovale into the left atrium According to Windle and Becker,[8] all or nearly all of the blood from the inferior vena cava passes through the foramen ovale, while blood from the superior vena cava streams through the right atrium into the right ventricle with little mixing of the two streams On the other hand, Everett and Johnson [9] who used more sensitive radioisotope techniques, reported that about one-fourth of the blood from each of the vena caval streams becomes mixed

Since the pulmonary venous return is relatively sparse, most of the oxygenated blood from the placenta flows directly into the left side of the heart to be pumped into the ascending aorta Thus, the first branches of the aorta receive blood with maximal oxygen content for delivery to the heart and the rapidly developing brain (Fig 6A) This mechanism is probably very important considering the fact that at least one orifice is normally present in the atrial septum at all stages of fetal development The blood flow through the pulmonary circulation probably increases as the lungs develop, but never even approaches the flow through the systemic circuit The output of the right and left ventricles is balanced by variations in the quantity of blood bypassing the lungs through the ductus arteriosus and through the orifices which persist in the interatrial septum (Fig 2) The flow of blood from the right into the left atrium and from the pulmonary artery into the aorta provides a functional demonstration of the fact that pressures in the right atrium, right ventricle and pulmonary artery exceed the pressures in the corresponding channels on the left This condition is the reverse of that seen shortly after birth

Postpartum Circulation

CARDIORESPIRATORY ADJUSTMENTS AFTER DELIVERY When the umbilical cord is severed after delivery, the infant's only source of oxygen is eliminated pending the establishment of effective respiratory exchange in the lungs Not only must air enter the lungs promptly, but blood flow through the pulmonary channels must be quickly augmented as well Ardran et al [10] demonstrated that the initial inflation of the lungs in fetal lambs was promptly followed by a precipitous fall in pressure in both the aorta and the pulmonary arteries (as much as 30 per cent of the initial pressure) This change was accompanied by a marked acceleration of flow through the pulmonary vascular tree, as would be expected from a reduced resistance to the flow of blood Tying the umbilical cord caused both pressures to rise together toward or above their initial level However as the ductus arteriosus closed, pressures in the pulmonary artery progressively fell below that in the aorta

CLOSURE OF THE DUCTUS ARTERIOSUS In the fetus, the tunica media of the ductus arteriosus is loose in structure, and composed of elastic fibers and smooth muscle [11] This histologic pattern is quite different from the compact tunica media of the other arterial trunks Very shortly after respiratory activity is initiated the ductus arteriosus closes down The prompt functional closure of the ductus arteriosus is probably due to contrac-

shunts form the basis for any logical approach to the diagnosis of congenital malformations of the heart

The Direction of Flow Through Simple Shunts

In the normal person, the pressures in the right atrium right ventricle and pulmonary artery are lower than the corresponding pressures in the left atrium ventricle and aorta As indicated in Chapter 4 the very slight resistance to flow through the vascular system in the lungs is the fundamental reason for the low pressures in the pulmonary artery and right ventricle The pressure in the right atrium is lower than that in the left because the thin walled right ventricle is more easily distended than the left during diastolic filling So long as the pulmonary resistance remains low in relation to systemic resistance and the right ventricular chamber remains normally distensible the pressures in all the channels leading to the lungs are lower than those in corresponding channels leading to the systemic vascular tree

Under these conditions the pressure differences promote the flow of blood *from the* systemic to the pulmonary circuit through any communication between *them as* illustrated schematically in Figure 7 The quantity of blood passing through such simple shunts depends upon the *pressure* difference across the shunt and the resistance to flow through it The resistance to flow is determined primarily by the caliber *of the* aperture or channel The principles governing the flow through shunts are the same as those applying to valve orifices (Fig 7, Chapter 18) The applicability of these concepts to various types of shunts will become apparent during the following discussion

Defects in the Interatrial Septum

The most common congenital malformation of the heart is a functionally significant aperture in some part of the interatrial septum The large proportion of individuals (o per cent of the general population) with probe patency of the foramen ovale are not included in this group Most interatrial defects are located at some distance from the tricuspid valves in the general region of the *foramen secundum or foramen ovale* (Fig 8*A*) Another fairly common site is in the vicinity of the foramen primum (see Fig 2*E*) These defects range from simple apertures less than 1 cm in diameter through multiple defects of varying size to virtual absence of the interatrial septum

FUNCTIONAL EFFECTS OF ATRIAL SEPTAL DEFECTS As indicated in the preceding section, the pressure in the left atrium generally exceeds right atrial pressure so long as the right ventricle is more distensible than the left For this reason the predominant flow through atrial septal defects is from the left atrium into the right The pressure difference between atria connected by an interatrial septal defect has been measured directly both in man[19] and in experimental animals 0 Left atrial pressure exceeded right atrial pressure at all times except for *transient* reversal of the pressure gradient, usually at the beginning of atrial systole Since the right atrial wall is excited first, pressure may build up faster in the right atrium than in the left This mechanism could account for brief periods of reversed flow through the shunt during each cycle producing very slight unsaturation of the arterial blood During rapid ventricular filling the atrial pressure difference diminishes or disappears[19]

The maximal recorded pressure differences between the right and left atria *ordinarily* range up to 6 or 8 mm Hg but the differences remain considerably below these levels during most of each cycle These pressures do not sound particularly impressive until it is recalled that the pressure gradient along a 1 or 2 cm *stretch of* the aorta or vena cava is imperceptible even when recorded by extremely sensitive apparatus. *Yet, these* minute pressure gradients propel the whole cardiac output along the main vascular trunks Thus, a pressure gradient *of* 3 or 4 mm Hg produces a

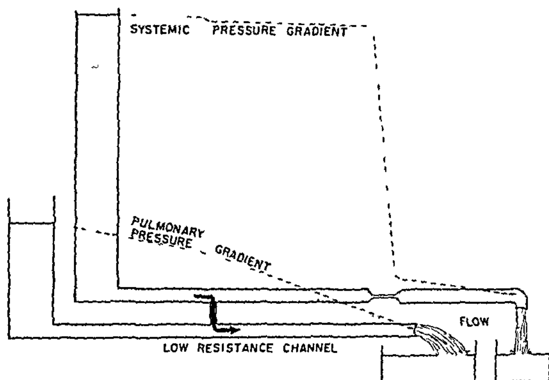


FIGURE 7 Beginning very soon after delivery, the resistance to flow through the pulmonary circuit becomes very low while the total peripheral resistance in the systemic circuit rises The pressures in the left ventricle and aorta greatly exceed corresponding pressures in the right ventricle and pulmonary artery so long as the pulmonary vascular bed remains a low resistance channel These large pressure differences propel oxygenated blood through communicating channels from the systemic system into the pulmonary circuit So long as pulmonary resistance remains low pulmonary blood flow can be greatly increased with little change in pulmonary arterial pressure The flow through abnormal channels connecting the pulmonary and systemic channels depends upon the size of the orifice and the magnitude of the pressure difference

signs and symptoms of congenital deformities are usually not at all characteristic during the first few months of life One explanation for these observations is that the pulmonary and systemic pressures remain fairly similar so that little or no blood flows through communicating channels between the systems The typical signs do not appear until the pressure differences become sufficient to propel large quantities of blood through the abnormal apertures

SIMPLE SHUNTS

The most common developmental defects in the heart and great vessels are incomplete partitioning of the pulmonary from the systemic circulation During the development of the septa dividing the heart and truncus arteriosus, apertures may persist leaving orifices at various sites in the walls separating the atria, ventricles and arterial trunks, as indicated in Figures 2 and 3 The foramen ovale and the ductus arteriosus normally remain functional until after delivery, and incomplete closure of these shunts is among the most common developmental defects The functional effects of the different simple shunts are remarkably similar whenever they occur as isolated lesions, uncomplicated by other developmental or acquired pathologic changes The principal effect of any of these communications between the systemic and pulmonary circuits is the recirculation of oxygenated blood back through the lungs producing abnormally large pulmonary blood flow The factors determining the direction of blood flow through simple

for months or years Immediately after birth the right ventricle has a relatively thick wall and functions under a pressure load similar to that of the left ventricle since the pressures in the pulmonary and systemic arterial systems are similar Thus there is little or no pressure gradient between the chambers and insignificant quantities of blood pass through the interatrial shunts As the pulmonary arterial resistance falls and systemic peripheral resistance rises the pressure differences between the two systems become greater The left ventricle becomes thick-walled and the right ventricle becomes more distensible as its pressure load diminishes Flow through interatrial communications then increases greatly in response to the steeper pressure gradients across the inter atrial partition The intensity of the murmur appears to bear some relation to the volume flow through the interatrial defect However the sounds are actually due to the rush of abnormally large quantities of blood through the pulmonary conus Thus this systolic murmur is produced by the same mechanism that causes "functional" murmurs (see Fig 16 Chapter 13) This fact was graphically demonstrated by phonocardiograms recorded directly from the surface of a dog's heart in which an interatrial septal defect had been produced surgically Although a very distinct systolic murmur promptly appeared over the pulmonary conus and pulmonary artery no murmur was recorded over either the right or the left atrium[22] In patients the murmur often attains such intensity that it is widely transmitted over the precordium and is associated with a thrill palpated in the pulmonary area Diastolic murmurs in the pulmonary area may result from dilatation of the pulmonary artery producing incompetence of the pulmonary valve

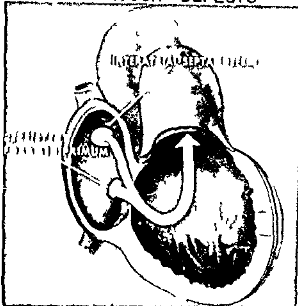
Fluoroscopy In most patients with functionally significant defects in the interatrial septum the pulmonary artery is dilated During fluoroscopic examinations of such patients in the postero-anterior position (see Fig 8B) a prominent bulge can be observed on the left border of the heart just above the cardiovascular angle Generally abnormally great pulsation of this dilated arterial trunk can also be observed Since it may be difficult to differentiate between simple displacement of the artery and expansile pulsation the peripheral lung fields should be carefully examined for increased pulsation of the smaller ramifications of the pulmonary arterial tree During this portion of the examination the x ray beam is restricted to a small area in the peripheral lung fields (dotted square in Fig 8B) and the vascular markings are watched carefully for signs of increased pulsation Expansile pulsation of the pulmonary artery and its branches may be increased by either increased blood flow or increased pulse pressure Frequently both factors are present in patients with interatrial septal defects or other types of simple shunts

Roentgenography In most patients with interatrial defects the right ventricle becomes enlarged because of the increased volume load (increased pulmonary blood flow) often supplemented by an increased pressure load (pulmonary hypertension) Roentgenographic evidence of anterior protrusion of the enlarged right ventricle is most easily observed when the patient is in the left anterior oblique position (see Fig 13 Chapter 11) Usually the right atrium is also enlarged but this is often difficult to demonstrate roentgenographically Angiocardiography is not generally recommended as a helpful diagnostic procedure in patients with simple septal defects However, Lind and Wegelius[23] have reported surprisingly good results using simultaneous biplanar exposures taken at rates of 10 to 12 per second

Electrocardiography In patients with atrial septal defects the right atrium usually becomes somewhat enlarged and the P waves in leads I and II are tall and peaked (see Fig 23 Chapter 15) The P waves on precordial leads are also affected by right atrial dilatation[24] Electrocardiographic signs of right ventricular hypertrophy are generally present but are usually somewhat obscured by atypical QRS complexes The sequence

INTERATRIAL SEPTAL DEFECTS

A FLOW THROUGH DEFECTS



B ROENTGENOGRAM (P-A)



FIGURE 8 *A* Interatrial septal defects most commonly occur in the region of the foramen ovale Occasionally the foramen primum fails to close (see Fig 2) In either case oxygenated blood surges from the left atrium into the right atrium and ventricle to be recirculated through the lungs along with the venous return from the systemic circulation

B The increased total pulmonary blood flow produces dilatation of the pulmonary artery which appears as a vigorously pulsating bulge on the left side of the mediastinum The pulmonary vascular markings are more prominent than normal Increased pulsation of the smaller branches of the pulmonary artery is observed by fluoroscopic examination of small areas in the peripheral lung field (e g dotted square) Right ventricular enlargement can usually be demonstrated fluoroscopically when the patient is rotated into the oblique positions (see Fig 13*C* Chapter 11) and on electrocardiograms (see Fig 22 Chapter 15) Dilatation of the right atrium is generally indicated by tall peaked P waves particularly in lead II (see Fig 23 Chapter 15) even when roentgenographic evidence is unconvincing

voluminous flow through apertures of similar dimensions in the interatrial septum The oxygenated blood that flows through the defect enters the right atrium and mingles with the returning systemic venous blood flowing to the lung (Fig 8) Thus the blood flowing through the shunt recirculates through the lung, increasing the total flow through the lung The quantity of oxygenated blood flowing into the left ventricle and pumped through the systemic arteries to the tissues is approximately normal, being controlled by complex neural and humoral mechanisms indicated in Chapter 5

Hickam[21] measured pulmonary blood flows of 15 to 20 l per minute in resting patients with simple atrial septal defects Thus, the right ventricular output was three or four times greater than left ventricular output These large volumes are propelled through the lungs by a pressure difference of only 12 or 13 mm Hg from the pulmonary artery to the left atrium In one patient blood flow of 15 l per minute was maintained through the pulmonary circuit by a pressure gradient of only 4 mm Hg Such tremendous flow produced by a small pressure gradient signifies that the pulmonary resistance remains very low

DIAGNOSTIC SIGNS OF ATRIAL SEPTAL DEFECT Clinical evidence of atrial septal defects stems primarily from the functional effects of greatly increased pulmonary blood flow and its secondary effects

Auscultation A loud systolic murmur in the pulmonary area on the precordium is usually the first clue to the presence of heart disease in patients with defects in the interatrial septum These murmurs are usually absent at birth and may not become audible

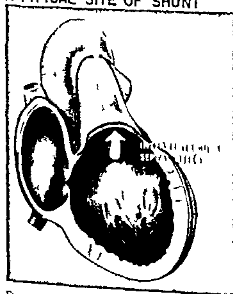
Extremely large flows through the shunt must result unless the ventricular septal defects are small or the pressure difference is greatly reduced

Interventricular defects are usually small and produce no functional disturbance of any kind The heart is normal in size and configuration, the pulmonary vascular markings are normal (Fig 9*B*) and exercise is well tolerated The presence of such small interventricular shunts is heralded by an extremely loud systolic murmur transmitted widely over the precordium but with greatest intensity in the third intercostal space at the left sternal border In most patients of this type minor ventricular conduction disturbances are observed electrocardiographically The P waves are usually normal in size and shape In contrast to the small shunts large interventricular septal defects profoundly affect the pulmonary circulation and will be considered along with other large simple shunts in subsequent sections (see *Simple Shunts with Pulmonary Hypertension* and *Acquired Cyanosis*)

Patent Ductus Arteriosus

If the ductus arteriosus fails to close part of the oxygenated blood ejected by the left ventricle surges through this shunt into the pulmonary artery and merges with venous blood passing out to the lungs The pressure difference across the ductus arteriosus can be extremely large ranging as high as 100

INTERVENTRICULAR SEPTAL DEFECT



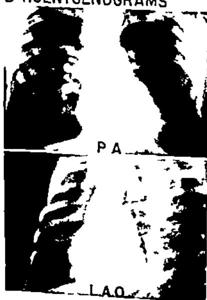


FIGURE 9 *A* Defects in the *interventricular* septum most frequently occur in the membranous septum just below the roots of the aorta and pulmonary artery This region corresponds to the interventricular foramen which is the last portion of the septum to be filled in (see Fig 3) Oxygenated blood surges through this orifice from the left ventricle at high velocity during systole because the difference in pressure between the ventricular cavities is very large. Loud coarse systolic murmurs are produced by the rush of blood through the restricted orifice They are widely transmitted over the precordium, but have maximum intensity in the third or fourth intercostal spaces along the left sternal border Diastolic murmurs are not generally audible

B Usually the interventricular defect is small and is not accompanied by symptoms of any kind The cardiac silhouette is normal in size and configuration, and the principal sign is the loud systolic murmur This picture conforms to the classic descriptions of Roger s disease However if the defect is large enough to be functionally significant, frontal roentgenograms often resemble those observed in patients with *atrial* septal defects The dilated, pulsating pulmonary artery is accompanied by increased pulmonary vascular markings Left ventricular enlargement may be demonstrable in the postero-anterior view and signs of both right and left ventricular enlargement may appear in the left anterior oblique view (see also Fig 14)

of ventricular excitation is apparently altered by an interventricular conduction disturbance For example, the R and S waves usually have almost equal amplitude in the precordial leads from V_2 to V_6, so the normal transitional zone is not apparent A deep S wave in lead I is often accompanied by a deep Q wave in lead III and the QRS complexes are frequently multiphasic The QRS interval is generally at or above the upper limits of normal for the age of the patients Such changes in QRS complexes may be associated with defects in either the interatrial or the interventricular septa, and are not very useful in distinguishing individual types of cardiac deformities However, they occur with sufficient regularity that they may lead to a suspicion of a congenital malformation even in young infants

Since all the simple shunts are characterized by abnormally increased pulmonary blood flow, they share many of the same clinical signs Although it is frequently possible to recognize the presence of an abnormal channel between the pulmonary and systemic circuits, its exact location often requires more direct demonstration by means of cardiac catheterization (see *Differential Diagnosis of Simple Shunts*) An accurate diagnosis of the exact site and nature of the lesion before attempting corrective surgery is very important because only certain types of defects are amenable to current surgical techniques Thus, various methods are being developed[25 29] for closure of atrial septal defects, but aberrant right pulmonary veins, which produce an identical clinical picture, present an entirely different surgical problem

Aberrant Right Pulmonary Veins

The veins draining the right lung normally empty into the left atrium very near the interatrial septum It is not surprising that as a result of defective development, the right pulmonary veins occasionally empty into the right atrium Aberrant right pulmonary veins drain fully oxygenated blood from the right lung into the right atrium This has precisely the same functional effects as the shunting of the same quantity of oxygenated blood through an interatrial septal defect For this reason, the clinical signs and symptoms of the two conditions are identical[30] Furthermore, an interatrial septal defect and aberrant pulmonary veins are frequently seen in the same patient, with functional effects corresponding to those of a very large atrial septal defect In this regard, a recent symposium on anomalous pulmonary venous connection and drainage is well worth reading[31] Rarely, all the pulmonary veins drain into the right atrium, a condition producing a quite different set of symptoms and signs which will not be considered here

The presence of right pulmonary veins emptying into the right atrium can be demonstrated only by inserting the tip of a cardiac catheter, under direct fluoroscopic control, into such a vein and withdrawing fully oxygenated blood from the channel (see Fig 11*B*)

Ventricular Septal Defects

During the last stages of partitioning in the heart, an aperture in the interventricular septum persists (Fig 2*F*) Endocardial cushion tissue proliferates into this aperture and later thins out to form the membranous portion of the interventricular septum just below the origin of the aorta and pulmonary arteries Incomplete closure of this opening is the most common defect in the interventricular septum although apertures in the muscular portion of the septum are occasionally reported For example, Konar and Sen Gupta[32] described an isolated defect in the muscular interventricular septum near the apex of the heart

Functional Effects of Interventricular Septal Defects Through an aperture connecting the two ventricular cavities, oxygenated blood is propelled from the left ventricle into the right by pressure differences which can be very large during systole (e g 100 mm Hg) and relatively small during diastole (0 to 10 mm Hg)

system The volume of flow through the shunt is usually greatest during systole diminishing during diastole in response to the variations in pressure difference The high velocity flow of blood through the restricted channel into the larger pulmonary artery produces turbulence (see Fig 15 Chapter 13) Such turbulence is responsible for the vibrations audible during both systole and diastole

Escape of blood from the systemic arterial system tends to depress the diastolic pressure Since the oxygenated blood flowing through the ductus does not contribute to perfusion of the tissues left ventricular stroke volume is augmented to compensate for the shunted blood (Fig 10A) However the systolic pressure in the systemic arteries is not usually elevated in patients with patent ductus arteriosus.

CLINICAL SIGNS OF PATENT DUCTUS ARTERIOSUS The volume of flow through a *small* ductus arteriosus is not sufficient to require any compensatory mechanism to maintain normal blood flow through the systemic circulation Left ventricular output is readily increased to provide normal systemic flow plus the small quantity of blood which escapes through the shunt The slight increase in left ventricular dimensions is often not apparent from roentgenographic examination (Figs 10*B* *C*) the electrocardiogram is within normal limits the arterial blood pressure remains normal and the only obvious sign is the characteristic murmur (Fig 10*D*)

Auscultation The most distinctive sign of patent ductus arteriosus is the continuous murmur The pressure difference between the aorta and the pulmonary artery persists throughout the cardiac cycle but is greatest during systole Thus the velocity of flow the degree of turbulence and the intensity of the resulting murmur reach a maximum during late systole and progressively diminish during diastole In contrast to the systolic and diastolic murmurs associated with semilunar valvular disease (Figs - and 4 Chapter 18) there is neither an interruption of the murmur nor a change in quality of the sound at the transition between systole and diastole For this reason the continuous quality of the murmur is quite distinctive Furthermore the murmur is best heard high on the left precordium usually in the left infraclavicular area In a large proportion of patients the characteristic murmur is the only definite sign of the lesion In about 10 per cent of patients the diastolic component of the murmur is either inaudible or absent This usually signifies elevated pulmonary pressure retarding the flow of blood through the ductus during the diastolic interval

Roentgenography If the ductus arteriosus is narrow the size and configuration of the cardiac silhouette are usually normal except for a bulge on the left border which signifies dilatation of the pulmonary artery The dilated pulmonary trunk and the peripheral vascular markings often exhibit expansile pulsation to an abnormal degree as in other types of simple shunts Even though the left ventricular stroke volume must increase to compensate for the shunting of blood from the systemic arterial system left ventricular enlargement is usually not great enough to be readily distinguished roentgenographically

Systemic arterial blood pressure A *small* ductus arteriosus produces some reduction in total peripheral resistance similar to the effects of vasodilatation in peripheral vascular beds The systemic arterial blood pressure remains within normal limits during both systole and diastole A *large* ductus arteriosus allows blood to escape from the arterial system so rapidly that the diastolic pressure may be depressed to levels of 50 to 60 mm Hg

SURGICAL TRANSECTION OF PATENT DUCTUS ARTERIOSUS During the past 15 years techniques of intrathoracic surgery have developed to the point that in most cases the ductus arteriosus can be ligated and transected with remarkably little hazard to the patient On rare occasions the ductus arteriosus is so large and friable that a

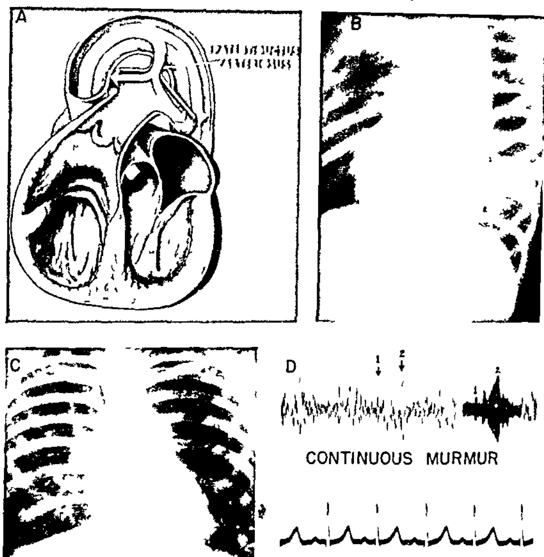


FIGURE 10 *A* If the ductus arteriosus remains patent the high pressure in the aorta forces oxygenated blood into the pulmonary artery increasing pulmonary blood flow

B The configuration of the cardiac silhouette in the left anterior oblique position conforms to the outline of the schematic drawing in *A* If the ductus arteriosus is small the cardiac silhouette may remain within normal limits when viewed from this angle Since left ventricular stroke volume is generally increased the movements of the left ventricular wall are somewhat exaggerated a sign which may be distinguished during fluoroscopy

C In many patients the size and configuration of the cardiac silhouette are entirely normal Dilatation of the pulmonary artery with normal or increased pulmonary vascular markings can often be demonstrated in the postero-anterior view Left ventricular enlargement is indicated by elongation of the heart (see Fig 11 Chapter 11) Definite evidence of cardiac enlargement generally signifies that the ductus arteriosus is large (see also Fig 14)

D The most characteristic sign of patent ductus arteriosus is a continuous murmur which begins shortly after the first heart sound gains intensity during late systole and diminishes during diastole This murmur has maximal intensity in the left infraclavicular region The electrocardiogram is usually within normal limits

mm Hg during systole and around 70 mm Hg during diastole The signs and symptoms of a small persistent ductus arteriosus are distinctly different from those resulting when this channel has large caliber, just as in the case of interventricular septal defects (see *Simple Shunts with Pulmonary Hypertension* and *Acquired Cyanosis*)

FUNCTIONAL EFFECTS OF PATENT DUCTUS ARTERIOSUS The ductus arteriosus serves as a low-resistance channel through which blood gushes out of the systemic arterial

ever large defects in the interventricular septum produce signs and symptoms much like those associated with other simple shunts The pulmonary artery may become dilated pulmonary vascular markings are accentuated and pulsate vigorously, and both right and left ventricles may become enlarged to different degrees

Interatrial septal defects and aberrant right pulmonary veins are functionally identical and usually cannot be distinguished by routine clinical methods Small interatrial septal defects probably produce no clinical sign whatever (not even a significant murmur)

In view of the functional similarity of the

DIFFERENTIAL DIAGNOSIS OF SMALL SHUNTS

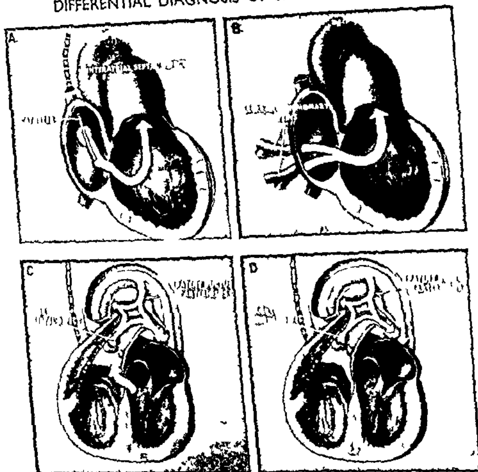


FIGURE 11 *A* The oxygen content of blood samples withdrawn from a catheter in the right atrium is higher than that of blood from the venae cavae if an interatrial septal defect is present.

B If right pulmonary veins empty into the right atrium, the oxygen content of blood in this chamber is elevated just as with an atrial septal defect. The only convincing method of distinguishing between these two conditions consists of inserting the *tip of the catheter* into the pulmonary vein or into the atrial septal defect under fluoroscopic control. This feat can be accomplished in a fairly large proportion of patients.

C The functional similarities of an interventricular septal defect, aortic septal defect and patent ductus arteriosus are indicated in this schematic *representation. Defects* in the interventricular septum are generally characterized by loud systolic murmurs over the lower precordium, without audible diastolic murmurs The shunts between the aorta and pulmonary artery generally cause "continuous murmurs" (see Fig 10) and may also diminish systemic arterial diastolic pressure and widen the pulse pressure.

D Patent ductus arteriosus and aortic septal defects are functionally identical and may not be distinguished by cardiac catheterization, since the shunts are in the same region. The principal point of distinction is the fact that patent ductus arteriosus is much more common than aortic septal defects

surgeon feels obliged to withdraw without attempting to close the vessel Although many patients with small shunts develop normally and have a normal life span, it is quite clear that patency of the ductus arteriosus usually reduces the life expectancy and produces signs and symptoms from the abnormal load either during childhood or in adult life Thus, patients, particularly children and young adults, whose growth is retarded or who suffer excessive fatigue or *signs of heart failure from this cause* are candidates for corrective surgery Subacute bacterial endocarditis is an indication for surgery after the infection has been treated optimally by antibiotics Appropriate therapy in patients who show *no evidence of* disability must be decided on the basis of the specific situation The advisability of prophylactic ligation of the ductus arteriosus must be decided by weighing the hazard of the operation against the probability of future disability and reduced life expectancy This problem has been discussed in detail by Gross and Longino [33]

Aortic Septal Defect

Although the clinical signs and symptoms of patent ductus arteriosus appear distinctive, this lesion cannot be differentiated from a functionally identical communication between the pulmonary artery and the aorta During the partitioning of the truncus arteriosus by the proliferating spiral aorticpulmonary septum (see Fig 3) incomplete fusion may leave a residual aperture just above the semilunar valves Fortunately, *from* a diagnostic point of view, this aortic septal defect is rare When it occurs, blood from the aorta surges through into the pulmonary artery during both systole and diastole The resulting continuous murmur is just like that heard in a patient with patent ductus arteriosus It is frequently stated that the greatest intensity is heard *lower on the precordium* (e g in the third *intercostal space* to the left of the sternum) when the murmur results from an aortic *septal defect This point of distinction has* not prevented its being mistaken for a ductus arteriosus [34, 36] Gross[37] has reported surgical closure of an aortic septal defect *unexpectedly encountered in a patient* presumed to have a patent ductus arteriosus However, diagnosis is so rarely made and the technical difficulties are so great that this procedure is not likely to become routine

Differential Diagnosis of Simple Shunts

Because of the pressure differences between the systemic and pulmonary channels, simple communications between these systems characteristically result in abnormally large blood flow through the lungs Thus, dilatation *and abnormal pulsations of the* pulmonary artery and of the peripheral vascular markings in the lungs can occur in each type of defect described above However, certain characteristic features permit differentiation by routine clinical methods in "typical patients For example, whenever a characteristic continuous murmur is *heard on the upper left precordium of a* patient with evidence of increased pulmonary blood flow, he probably has a shunt between the aorta and pulmonary artery As pointed out above, this murmur is common to both a patent ductus arteriosus and an aortic septal defect which generally cannot be distinguished by available clinical methods *If the continuous murmur has max*imum intensity in the third intercostal space just to the left of the sternum the lesion is more apt to be an aortic septal defect Cardiac catheterization often fails to distinguish these two lesions (see Fig 11) Angiocardiography should give more definitive information but is rarely employed because an aortic *septal defect is usually not* considered

The usual descriptions of interventricular septal defects apply only to small shunts The heart remains normal in size and configuration because the flow through the small aperture is not sufficient to impose a load on either ventricle In such patients the *only sign is a loud systolic murmur* How-

slight that an arteriovenous pressure gradient of 4 to 6 mm Hg is sufficient to propel not only the normal resting flow through the lungs (4 to 5 l per minute) but as much as three times this amount with no increase in pulmonary arterial pressure[4] In the systemic circulation the same volume flow is propelled from the aorta to the venae cavae by a mean arteriovenous pressure difference of some 90 mm Hg or more Thus the normal resistance to flow through the systemic circuit must be some 15 times greater than pulmonary vascular resistance

The significance of this fact becomes apparent in considering a heart with a very large interventricular septal defect In such a case the right and left ventricles function more or less like a single ventricular chamber Since the blood ejected from this chamber can go into either the pulmonary artery or the aorta the quantity entering each vessel is determined by the relative resistance to flow through the two vascular systems Clearly the preponderant flow would pass through the low resistance pulmonary circuit (Fig 12*A*) If the pulmonary resistance diminished and systemic resistance increased to the normal extent in an infant with this condition the systemic resistance might well exceed pulmonary resistance by tenfold The systemic blood flow would be only one tenth the pulmonary blood flow Thus normal perfusion of the tissues would require a total ventricular output about ten times normal Such tremendous output is beyond the capacity of the ventricles and the infant would not survive However pulmonary resistance at birth is approximately equal to systemic resistance If a balance between pulmonary and systemic resistance were maintained the systemic and pulmonary flow would be equalized even with a large defect in the partitions of the heart (Fig 12*B*) Since the systemic resistance always progressively increases after birth the maintenance of abnormally high pulmonary resistance is essential for survival in the presence of large apertures between the ventricles and arterial trunks

Causes of Pulmonary Hypertension

In the fetus the walls of the pulmonary arteries have thick muscular coats (which normally thin out during early childhood) The pulmonary resistance actually exceeds systemic resistance and pulmonary blood flow is much less than systemic flow Thus even large shunts produce little circulatory disability in the fetus Immediately after birth pulmonary resistance normally diminishes progressively and systemic resistance rises During this adjustment many infants expire For example, of 1000 live infants with congenital malformations of the heart nearly half died within the first month[43] Presumably, many patients die because the heart cannot sustain either the required volume or the required pressure load abruptly imposed during the conversion from the fetal type of circulation The high pulmonary resistance may persist longer than normal in

THE SIGNIFICANCE OF PULMONARY HYPERTENSION

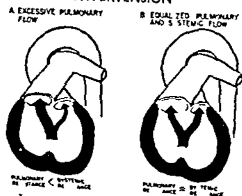


FIGURE 12 *A* The pulmonary vascular resistance is greatly increased when there are large shunts in the partitions of the heart. The functional importance of the response is illustrated by an extreme example in which the interventricular septum failed to form (see Fig 2*C*) Blood ejected from the single ventricle would tend to flow predominantly in the pulmonary artery since this circuit offers the least resistance If the pulmonary resistance were only 1/10 that of the systemic circuit a correspondingly small fraction of the total ventricular ejection would enter the aorta to perfuse the tissues Usually pulmonary blood flow exceeds systemic flow by only three or fourfold indicating that pulmonary resistance is much higher than the normal values

B The flow through the systemic and pulmonary circuits can be the same only if the pulmonary resistance equals systemic arterial resistance

various simple shunts, a definitive diagnosis often requires cardiac catheterization The presence of a left to right shunt can be detected by inserting the catheter into the pulmonary artery and then withdrawing blood samples through the catheter as its tip is moved under fluoroscopic control into different positions in the pulmonary arteries, right ventricle, right atrium and venae cavae The flow of oxygenated blood through a shunt elevates the oxygen saturation both near the orifice and beyond it

Changes in blood oxygen saturation serve to localize the shunts to arterial trunks, ventricles or atria, but fail to distinguish between patent ductus arteriosus and aortic septal defects, or between interatrial septal defects and aberrant right pulmonary veins These shunts can be more accurately localized by inserting the catheter through the orifice or channel (Fig 11)

Additional valuable information concerning the site and magnitude of shunts is now being obtained by means of indicator dilution curves If a dye is injected into a peripheral vein and the changes in its concentration in a peripheral artery are continuously registered, a curve of increasing and decreasing concentration of the dye can be recorded The configuration of this dye concentration curve is altered by the presence of shunts By injecting the dye through a catheter with its tip at various locations in the pulmonary arteries, right ventricle, right atrium and venae cavae, the changes in the contour of the recorded curves can be interpreted to provide information concerning the location of the aperture and the amount and direction of flow through the abnormal channels If the dye is injected distal to the site of a defect, the blood traverses normal pathways and a normal pattern is recorded If material is injected proximal to a defect some of the dye will either be shunted through the defect or diluted by blood traversing the shunt in the opposite direction through the abnormal channel This technique is particularly valuable for detecting shunts through which blood flows only from the right side of the heart into the systemic circulation [38] In such patients oxygen saturation within the right chambers and the pulmonary artery is not affected

In the presence of interatrial septal defects or aberrant right pulmonary veins the curves produced by injecting the dye first into the left pulmonary artery and then into the right are different because flow into the right atrium is predominantly from the right lung rather than from the left [39] For additional information on this subject the reader is referred to original publications of Wood and his associates [38-41]

In most patients with significantly increased pulmonary blood flow, the systolic pressures in the pulmonary artery and right ventricle are elevated The pressures may be in the upper range of normal or far above normal levels Generally, normal pressures are recorded from catheters wedged in peripheral pulmonary arterial branches This indicates that the principal cause of the pulmonary hypertension is increased resistance to the flow of blood through the pulmonary arterial system Since increased pulmonary resistance may grossly affect the signs and symptoms generally found with simple uncomplicated shunts, the hemodynamic alterations associated with pulmonary hypertension deserve consideration

SIMPLE SHUNTS WITH PULMONARY HYPERTENSION

The classic signs and symptoms of the various shunts described in preceding sections actually apply only to small or moderate-sized communications The quantity of blood flowing through such shunts constitutes no immediate threat to survival However, large defects particularly those between the ventricles and arterial trunks can transmit such large portions of the total left ventricular output into the pulmonary circuit that the patients cannot long survive unless flow through the lungs is severely restricted

Normally the pulmonary resistance is so

above 5 gm per cent the bluish color characteristic of venous blood replaces the pinkish hue in these areas This bluish tinge or cyanosis must be explained in terms of the factors which increase the quantity of reduced hemoglobin in the small cutaneous vessels

If arterial unsaturation with cyanosis persists for long periods a bulbous enlargement of the terminal phalanges on the fingers and toes develops In this condition called clubbing the configuration of the distal phalanges changes from a roughly cylindrical to a more spherical shape The nails develop a pronounced longitudinal curvature The cause of clubbing is not known

Etiology of Cyanosis

The quantity of reduced hemoglobin in the venous blood from any particular tissue depends upon four factors (*a*) the total hemoglobin concentration in the blood (*b*) the quantity of reduced hemoglobin in the arterial blood (*c*) the rate of blood flow through the tissue and (*d*) the rate of oxygen utilization by the tissue For reasons pointed out above blood in the cutaneous vessels usually contains very little reduced hemoglobin (about 1 or 2 gm per cent) (see Fig 3 Chapter 5) The concentration of reduced hemoglobin in these vessels can increase as a result of either retarded blood flow or abnormally high levels of reduced hemoglobin in the arterial blood If arterial blood contains reduced hemoglobin in excess of 3 to 4 gm per cent the normal oxygen uptake in the skin may well increase the total quantity of reduced hemoglobin in cutaneous vessels above the critical level of 5 gm per cent. Whenever cyanosis occurs during rapid cutaneous blood flow the arterial blood must contain abnormally large quantities of reduced hemoglobin In patients with developmental defects in the heart cyanosis results primarily from the flow of unsaturated venous blood through the defect to mix with the arterial blood

The amount of venous admixture required to produce cyanosis is related to the quantity of blood being oxygenated by the lungs Under some conditions, the entire systemic venous return mixes with the blood returning from the lungs without producing cyanosis As an oversimplified example consider a patient in whom the interventricular septum failed to develop (Fig 13) Blood returning from the systemic veins and from the lungs mixes within a single ventricular chamber and is then ejected into both the pulmonary artery and the aorta In such cases it is rather common for the pulmonary blood flow to be three times as large as systemic flow If five liters of systemic venous blood (6 7 gm per cent reduced hemoglobin) were completely mixed with 15 liters of fully oxygenated blood from the lungs, the arterial blood would contain only 1 7 gm per cent of reduced hemoglobin During flow through the cutaneous vessels extraction of 1 or 2 gm per cent more hemoglobin would be insufficient to produce cyanosis (*see Fig 13A*) Although the quantity of reduced hemoglobin in mixed venous blood from the systemic veins is higher than normal (6 7 gm per cent) there would be no cyanosis because this blood is mixed with such a large volume of fully oxygenated blood from the lungs Similarly if pulmonary blood flow were just twice systemic flow (*Fig 13B*) the mixed blood leaving the single ventricle would contain only 2 5 gm per cent of reduced hemoglobin Although a patient with this degree of arterial unsaturation might not display cyanosis under resting conditions he would develop cyanosis more easily during retarded blood flow in the skin (*crying*) or during greater oxygen consumption and unsaturation of the systemic venous blood (e g exercise) Furthermore cyanosis would be more readily visible if the cutaneous vessels were engorged with blood If pulmonary and systemic flows were equal (pulmonary resistance = systemic resistance) the mixed blood in the arteries would contain 5 gm per cent reduced hemoglobin and cyanosis would surely result (Fig 13C) If pulmonary blood flow were diminished to one half of the systemic flow

infants surviving with large shunts, and flow through the *shunts may be absent or in the* reverse direction from that observed in older individuals The causes of high pulmonary resistance must be sought among the factors which produce pulmonary constriction[44-46]

Histologic changes in the walls of pulmonary arterial branches are generally demonstrable in patients with persistent severe pulmonary hypertension Edwards and his associates[47-49] have repeatedly reported finding extensive hypertrophy of the media in the muscular arteries within the lungs of patients with large shunts between the ventricles or arterial trunks This hypertrophy was often accompanied by fibrosis of the intima They have emphasized the similarity between the pulmonary arteries in such patients and in the normal fetus, suggesting that *the former may represent* a carry-over from fetal life However, many such patients fail to develop evidence of severe pulmonary hypertension until later in life, often after reaching maturity

Paul Wood[50] was impressed with the fact that the incidence of pulmonary hypertension ranged around 20 per cent in his series of patients suffering from different conditions including atrial septal defects, ventricular septal defects, patent ductus arteriosus and mitral stenosis On this basis he proposed that approximately 20 per cent of such persons react to pulmonary congestion or increased pulmonary blood flow in a vigorous and vicious manner, developing pulmonary hypertension, while others tend to decrease pulmonary resistance in response to increased pulmonary flow The incidence of pulmonary hypertension is not uniform in different series reported For example, Swan et al [51] reported mean pulmonary arterial pressures in excess of 40 mm Hg in only 1 of 24 patients with atrial septal defects, 14 of 20 patients with ventricular septal defects, and 10 of 24 patients with patent ductus arteriosus Significantly, they observed that the pulmonary blood flow was similar in the three groups Thus the degree of pulmonary hypertension appears to reflect an increase in pulmonary *resistance sufficient to restrict the total out*put of the ventricles to a level within their capacity

If the pulmonary arterial resistance exceeds total systemic resistance, flow through *the shunt is reversed, forcing unsaturated* blood from the pulmonary circuit into the systemic circulation This circulatory pattern resembles that observed in the normal fetus (Fig 6) Flow of unsaturated blood through simple shunts into the systemic circulation has been most frequently reported in patients suffering from patency of the ductus arteriosus[52-56] However, similar effects also result from other large simple shunts such as large interventricular septal defects (*vide infra*) and interatrial septal defects[57, 58] If sufficient quantities of unsaturated blood *returning from the systemic veins are shunted* into the systemic arterial system, a bluish discoloration of the skin, mucous membranes and nailbeds, called cyanosis, becomes visible

ACQUIRED CYANOSIS

Normally, 100 ml of blood contains about 15 gm of hemoglobin, which is *almost com*pletely saturated with oxygen when it leaves the lungs While the oxygenated blood flows through the systemic capillary networks, some oxygen diffuses into the tissues, part of the oxyhemoglobin being converted to reduced hemoglobin Typical venous blood contains about 5 mg per cent of reduced hemoglobin which is *responsible for its bluish* color Because of the voluminous blood flow through the skin, so little oxygen is extracted that the amount of reduced hemoglobin within the cutaneous capillaries is only slightly larger than that in arterial blood In the normal individual the red-colored oxyhemoglobin in the capillaries and *venules of the skin is responsible* for the pink flesh tones, particularly where dense vascular networks are near the surface (e g, lips, mucous membranes, nailbeds, cheeks) If the quantity of reduced hemoglobin in these cutaneous vessels rises

from systemic veins with 8.5 gm. per cent reduced hemoglobin is mixed with 5 liters of arterial blood per minute. Under these conditions systemic flow greatly exceeds pulmonary flow. Smaller volumes passing from right to left through the shunt would produce cyanosis only if oxygen consumption increased (more reduced hemoglobin in mixed venous blood) or systemic blood flow were diminished.

Although these examples are oversimplified, their interpretation leads to two important generalizations. (*a*) If pulmonary blood flow exceeds normal systemic flow by twofold or more, cyanosis is not likely even with complete mixing of the total systemic and pulmonary venous return. (*b*) Cyanosis develops in patients with large unidirectional right to left shunts when pulmonary blood flow is significantly below systemic blood flow. In the presence of a large shunt between the ventricles or arterial trunks, pulmonary flow is less than systemic flow only when pulmonary resistance exceeds systemic resistance. Thus the factors which lead to pulmonary hypertension (increased pulmonary resistance) also promote the development of cyanosis if the pulmonary vascular changes become excessive.

In addition to the factors considered above, the total concentration of hemoglobin in the blood affects the development of cyanosis. For example, a patient with severe anemia is less apt to develop cyanosis since a much greater proportion of the hemoglobin must be relieved of oxygen to produce 5 gm. per cent of reduced hemoglobin. In this process the oxygen tension in the blood would be lowered to an extreme degree. This unfavorable condition is avoided by acceleration of systemic blood flow (increased cardiac output). Conversely, many patients with arterial unsaturation and cyanosis develop polycythemia. The total hemoglobin concentration in the blood is increased to abnormally high levels. Although polycythemia increases the oxygen capacity of the blood, a smaller drop in blood oxygen tension produces 5 gm. per cent of reduced hemoglobin and cyanosis is more apt to develop.

Differential Diagnosis of Shunts with Acquired Cyanosis

Since cyanosis in congenital malformations of the heart means that unsaturated blood from the systemic veins is entering the systemic arterial system, the direction of flow through the defects must be reversed. This means that the pressures in the channels leading to the lungs must exceed the corresponding pressures on the systemic side of the circulation. Most patients who acquire cyanosis as a result of large shunts with compensatory pulmonary hypertension have a history of transient or intermittent cyanosis extending over months or years during the time that the pulmonary resistance has built up. In some patients intermittent cyanosis is present from birth, indicating that the pulmonary resistance did not fall in the normal fashion after respiratory activity was initiated.

Atrial Septal Defects

Even large defects in the interatrial septum are fairly well tolerated. Indeed, complete absence of the septum may give rise to remarkably slight cyanosis. The increased volume flow through the lungs imposes a volume load on the right ventricle which is well tolerated. However, if pulmonary blood flow is excessive, pulmonary resistance increases and pulmonary hypertension develops. The right ventricle hypertrophies to compensate for the pressure load and its distensibility is reduced. If the diastolic pressure of the thick-walled right ventricle rises, right atrial pressure also increases. The right and left atrial pressures become equalized and the flow through the shunt diminishes or even reverses. Under these circumstances the systemic arterial blood contains some shunted venous blood and exhibits slight unsaturation. Catheterization may fail to demonstrate any significant shunt in either direction across the septal defect. Pressures in the pulmonary artery and right

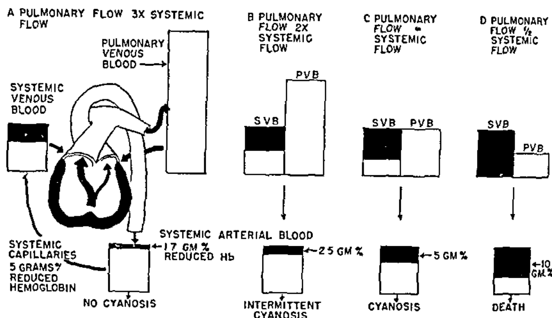


FIGURE 13 Cyanosis becomes visible when the blood in superficial vessels of the skin contains approximately 5 gm per cent of reduced hemoglobin The conditions under which cyanosis would appear when the systemic and pulmonary venous blood is completely mixed in a single chamber can be evaluated by making certain assumptions which are not always applicable First let us assume that during flow through the skin 2 gm per cent of oxyhemoglobin is converted to reduced hemoglobin by oxygen extraction in the skin capillaries Under these conditions the arterial content of reduced hemoglobin must be increased to 3 gm per *cent to produce a total of 5 gm per cent in the skin If oxygen consumption and the volume flow through the* systemic vessels are normal [19] the mixed systemic venous blood should contain 5 gm per cent more reduced hemoglobin than the arterial blood To simplify discussion assume that pulmonary venous blood is fully oxygenated and contains no reduced hemoglobin

A Under the conditions outlined above if the pulmonary blood flow is three times the normal systemic flow the mixture in the arterial blood would contain 1 7 gm per cent of reduced hemoglobin The additional 2 gm per cent of reduced hemoglobin acquired in the skin brings the level to 3 7 gm per cent of reduced *hemoglobin a quantity insufficient to produce cyanosis*

B If pulmonary blood flow were only twice the systemic flow the skin vessels would contain about 4 5 gm per cent of reduced hemoglobin so that an increase in oxygen consumption (e g exercise) or retardation of blood flow (crying) could produce visible cyanosis

C Equal flow through the systemic and pulmonary circuits (see Fig 12) would result in an arterial content of reduced hemoglobin of more than 5 gm per cent which should produce a cyanosis at rest that would become more severe under various conditions Note that the mixed venous content of oxygen is greatly depressed *indicating that the oxygen tensions in the tissues are probably greatly depressed*

D If pulmonary resistance increased so much that pulmonary flow was reduced to one half the systemic flow the arterial blood would contain 10 gm per cent of reduced hemoglobin (only 5 gm per cent of oxyhemoglobin) and mixed venous blood would be completely unsaturated Obviously this situation could not be survived

the arterial and venous blood would contain 10 and 15 gm per cent reduced hemoglobin, respectively (Fig 13D) *In other* words, the arterial blood would contain little oxygen and venous blood would contain none, a condition which would not support life unless cardiac output and oxygen carrying capacity of the blood were greatly increased

Cyanosis also develops in patients with large shunts through which blood flows from systemic veins into the left atrium left ventricle or aorta Under these conditions unsaturated blood, which would otherwise pass through the lungs for oxygenation escapes through the shunt and mixes with the systemic arterial blood In other words, the systemic flow is augmented at the expense of pulmonary blood flow If the oxygen consumption and total systemic blood flow remain normal, cyanosis would appear when some 2 liters of blood returning

ventricle tend to be elevated but not to very high levels At this stage systemic and pulmonary blood flows are often roughly equal Thus the circulatory compensation for a large interatrial septal defect tends to eliminate the characteristic signs of this condition The quantity of venous blood passing into the left atrium is frequently increased by exertion and during certain phases of the respiratory cycle If advantage is taken of these facts the presence of atrial defects may be more easily demonstrated during cardiac catheterization

Atrial Septal Defect with Pulmonary Stenosis

Defects in the interatrial septum often accompany stenosis of the pulmonary valve (see Fig 11 Chapter 18) In this condition, increased right ventricular systolic pressure is required to force the normal complement of blood through the stenotic orifice Thus the valvular stenosis places a pressure load on the right ventricle corresponding to the increased resistance which may develop in peripheral pulmonary arterial branches due to atrial septal defects alone If hypertrophy diminishes right ventricular distensibility the right atrial pressure may increase enough to reverse the normal pressure gradient and force unsaturated blood into the left atrium From a functional point of view there is no significant difference between localized valvular stenosis and generalized peripheral increase in pulmonary arterial resistance and these two conditions can often be distinguished only by catheterization A sharp pressure drop across the pulmonary valve region indicates local stenosis in this region (see Fig 11 Chapter 18) Angiocardiography in the right anterior oblique position often reveals a constricted region near the pulmonary valve if pulmonary stenosis is present Post-stenotic dilatation, abnormally low pulmonary flow and diminished pulmonary vascular markings are frequently observed

Large Defects in the Interventricular Septum

As indicated in the preceding discussion of pulmonary hypertension free communication between the right and left ventricles through a large defect in the ventricular septum can be survived only if the pulmonary resistance remains high The systolic pressure in the right ventricle and in the pulmonary artery are characteristically identical with systolic pressure in the systemic arteries even during changes in cardiac output (e g exercise) Although left ventricular output may have been grossly increased in the earlier stages by the time the pressures become equalized its ejection is probably normal Right ventricular hypertrophy and right atrial dilatation remain the predominant electrocardiographic signs Roentgenographic evidence of right ventricular hypertrophy pulmonary arterial dilatation and pulsation and increased pulmonary vascular markings is comparable to that in other types of acquired cyanosis with large simple shunts (Fig 14)

Eisenmenger s complex has been the tra-

B A large interventricular septal defect is functionally identical with the *Eisenmenger* complex

C Massive dilatation of the pulmonary artery greatly increased pulmonary vascular markings and enlargement of both right and left ventricles occur whenever a large shunt exists between either the ventricles or the arterial trunks

D Right and left ventricular enlargements are easily demonstrated in the left anterior oblique view Roentgenographic changes illustrated in C and D could occur in patients with any of the large shunts illustrated in this figure

E If the ductus arteriosus attains a caliber approaching or exceeding that of the aorta pulmonary hypertension must develop to prevent siphoning off of most of the total systemic flow When aortic and pulmonary arterial pressures are approximately equal blood flow through the shunt is diminished or absent during certain phases of each cycle The characteristic continuous murmur is often replaced by either systolic or diastolic murmurs (see text)

F A truncus arteriosus with a large pulmonary artery is fundamentally a very large aortic septal defect and has the same functional effects as a large ductus arteriosus

LARGE SHUNTS PRODUCING PULMONARY HYPERTENSION AND ACQUIRED CYANOSIS

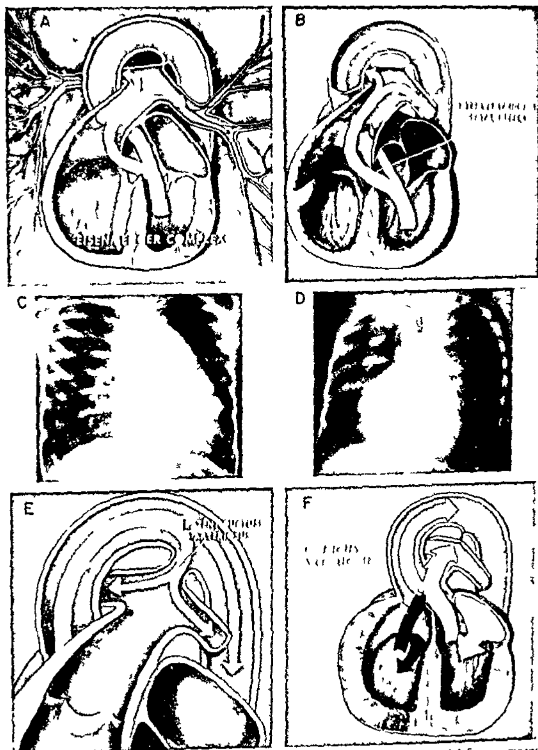


FIGURE 14 *A* The Eisenmenger complex is essentially a large interventricular septal defect accompanied by an apparent displacement of the aorta toward the right so that its orifice lies over the defect. So long as pulmonary resistance remains lower than total systemic resistance oxygenated blood from the left ventricle joins the systemic venous blood in the right ventricle and recirculates through the lung. The right ventricle becomes hypertrophied to compensate for the sustained pressure load. In response to the greatly increased pulmonary blood flow pulmonary resistance rises as indicated in Figure 12. The left ventricle must eject an abnormally large stroke volume and must dilate to compensate for the volume load. In many such patients pulmonary resistance ultimately exceeds systemic resistance so the shunt is reversed and unsaturated blood enters the aorta to produce cyanosis (see text)

ventricle tend to be elevated but not to very high levels At this stage, systemic and pulmonary blood flows are often roughly equal Thus the circulatory compensation for a large interatrial septal defect tends to eliminate the characteristic signs of this condition The quantity of venous blood passing into the left atrium is frequently increased by exertion and during certain phases of the respiratory cycle If advantage is taken of these facts the presence of atrial defects may be more easily demonstrated during cardiac catheterization

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ditional example of acquired cyanosis It consists of right ventricular hypertrophy, and interventricular septal defect with orifice of the aorta situated above the interventricular septum (overriding or dextroposed aorta), and cyanosis, usually developing around the time of puberty The ready access of blood from the right ventricle into an overriding aorta has been erroneously ascribed a role in the development of cyanosis in these patients Actually, blood ejected by the right ventricle follows the path of least resistance and enters the aorta in significant quantities only if the pulmonary resistance is as high as or higher than the systemic resistance The presence of an overriding aorta is not easily distinguished even *during pathologic examination* because a probe can be easily passed from the right ventricle into the aorta through *any large ventricular septal defect For these* reasons, there seems little justification for making a distinction between the Eisenmenger complex and any *other large inter*ventricular septal defect with cyanosis due to vascular changes in the lungs

Persistent Truncus Arteriosus

Complete absence of the spiral aortic *pulmonary septum is merely an exaggerated* form of aortic septal defect The functional effects are exactly the same as those of a *large interventricular septal defect so long* as a large pulmonary artery arises from the common trunk to supply the lungs Here *again, the pulmonary resistance must be* greatly elevated to provide a degree of balance between systemic and pulmonary flow *which is compatible with life The systolic* pressures in the right and left ventricles, truncus arteriosus, and aortic and pulmo*nary arteries are equal This lesion does not* characteristically produce cyanosis until pulmonary blood flow is diminished below *aortic flow, indicating that venous admixture* has occurred The pressures and blood oxygen saturation determined from catheters in the truncus *arteriosus are often* indistinguishable from those encountered with either a large interventricular septal defect or a large patent ductus arteriosus

Patent Ductus Arteriosus

The signs and symptoms of a *large* patent ductus arteriosus complicated by severe pulmonary hypertension differ greatly from those produced by small aortic-pulmonary shunts The distinctive 'continuous' murmur is generally absent, being replaced by a blowing diastolic murmur along the left border, a systolic murmur of varying intensity, or even no audible murmurs at all[55] The systemic arterial pressure is normal The heart is enlarged, usually from expansion of both the right and left ventricles Electrocardiograms *may indicate* either right or left ventricular preponderance However, another fairly characteristic *sign has been recently reported*[46 55] *Un*saturated blood passing through the ductus arteriosus from the pulmonary artery enters *the aorta at a point just beyond the origin of* the innominate artery and opposite or beyond the origin of the left subclavian and *left carotid arteries For this reason the de*gree of unsaturation of arterial blood is often demonstrably greater in the lower *extremities than in the right arm or head* If there is no demonstrable difference between arterial oxygen saturations in the *upper and the lower extremities under* ordinary circumstances it may be induced if the patient breathes gas mixtures with *low oxygen tensions The resulting increase* in pulmonary resistance fosters larger flow of unsaturated blood from the pulmonary *artery into the descending aorta* Because of the variable relationship between the ductus arteriosus and the vessels springing from the *aortic arch the exact peripheral* distribution of unsaturated arterial blood cannot be accurately predicted[46] *If dyes are injected into the peripheral vein or through a catheter* into the right side of the heart the dye entering directly into the aorta from the pulmonary artery can be distinguished in

the femoral artery and occasionally in progressively diminishing quantities in arteries more proximal on the aortic arch

DEVELOPMENTAL DEFECTS WITH INTRINSIC CYANOSIS

Cyanosis is such an obvious clinical sign that congenital malformations of the heart are usually divided into a cyanotic and a noncyanotic group However under certain conditions cyanosis develops in patients with simple shunts which are generally classified as noncyanotic (see *Acquired Cyanosis*) To this extent the common classification of these lesions causes unnecessary *confusion* Nevertheless cyanosis accompanies certain types of developmental defects with sufficient regularity that they can be grouped in the cyanotic category if it is recognized that even these lesions do not always produce cyanosis in all cases or at all times For example, some patients with these lesions develop cyanosis immediately after birth while others do not exhibit this sign for some months after delivery The widely diversified lesions which characteristically produce cyanosis have two features in common (*a*) defects in the partitions of the heart and (*b*) anatomic obstruction to the flow of systemic venous blood *into or* through the lungs The differential diagnosis of these defects is facilitated by always considering the site of the shunt and the nature and location of the obstruction to flow of venous blood into the lungs Variations in these two factors produces a bewildering array of malformations many of which are extremely rare For this reason a few of the more common examples will serve to illustrate the basic approach to their diagnosis

Tetralogy of Fallot

The most familiar congenital *defect* typically accompanied by cyanosis is the tetralogy of Fallot so named because *four main* items were included in the original description (*a*) a defect in the *membranous portion* of the interventricular septum (*b*) an overriding aorta in which the aortic orifice lies over the interventricular septum (*c*) pulmonary stenosis (valvular or infundibular) and (*d*) right ventricular hypertrophy Two of these four features are redundant An overriding aorta cannot occur without an interventricular septal defect and pulmonary stenosis regularly causes right ventricular hypertrophy Excluding the superfluous descriptive features the basic defects are interventricular septal defect and pulmonary stenosis which acts to obstruct the flow of unsaturated systemic venous blood into the lungs

Although the exact embryologic origin of this type of defect is *not established its* location suggests abnormal partitioning of the conus region by the *spiral* aortic-pulmonary septum (see Fig 15 *I*) If the ridges which ultimately form this spiral septum deviated toward *the right during* their original development the caliber of the outflow tract *from* the right ventricle would be reduced and the aortic orifice would be relatively large The spiral aortic septum could not fuse with the *proliferating inter*ventricular septum and an *interventricular* septal defect would be left directly below the origin of the aorta (an overriding aorta) This explanation is probably oversimplified *but it* gives some insight into the possible mechanisms underlying this defect It seems significant *that* most patients with *tetralogy of Fallot* have an infundibular type of *stenosis* rather than a *valvular stenosis although the latter does occur* Valvular stenosis also could *result* from a deviation *of the* spiral *septum* to the right producing an asymmetric division of the endocardial cushions which ultimately form the pulmonary valves (see Fig 4)

FUNCTIONAL EFFECTS OF TETRALOGY OF FALLOT The pulmonary stenosis *impedes* the flow of blood into the pulmonary artery To provide a steeper pressure gradient across the restricted pulmonary orifice, right ventricular pressure must reach abnormally high levels Because of the large interventricular septal *defect* the right ventricular systolic pressures equal left ventricular

TETRALOGY OF FALLOT

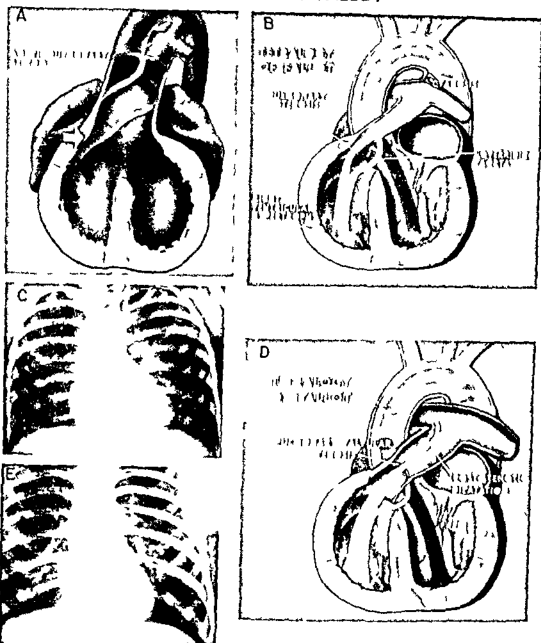


FIGURE 15 *A* If the lower portion of the spiral aortic pulmonary septum deviated toward the right during its development the infundibular portion of the right ventricle would be constricted and the aorta would override the interventricular septum This schematic diagram is probably oversimplified but it illustrates a mechanism by which the tetralogy of Fallot could develop

B The tetralogy of Fallot is characterized by an infundibular type of pulmonary stenosis overriding of the aorta a large interventricular septal defect and right ventricular hypertrophy Because of the increased resistance to flow past the infundibular obstruction into the lungs cyanosis generally develops during the first weeks or months of life

C The outflow tract of the right ventricle and the pulmonary trunk are usually diminished in size so the left border of the cardiac silhouette is concave in the frontal view The vascular markings in the peripheral lung fields are greatly reduced The hilar shadows are often quite prominent but appear disorganized probably owing to the presence of dilated bronchial arteries which serve to supplement pulmonary blood flow (see text) Right ventricular hypertrophy can be demonstrated by rotating the patient into the left anterior oblique view (see *B* above)

D In a small proportion of patients with tetralogy of Fallot the pulmonary valve is stenotic with or without an accompanying infundibular type of stenosis Valvular stenosis may also result from unequal partitioning of the truncus arteriosus by deviation of the spiral aortic pulmonary septum (see *Fig* 4) The functional effects of valvular and infundibular stenosis are the same so the clinical pictures are correspondingly similar

E Pulmonary valvular stenosis is often accompanied by post-stenotic dilatation of the pulmonary artery (see Fig. 11 *A*, Chapter 18), which appears as a prominent bulge on the left side of the mediastinum.

pressure If resistance to flow through the stenotic region into the pulmonary artery is sufficiently great unsaturated blood from the right ventricle joins the oxygenated blood from the left ventricle entering the aorta for distribution throughout the systemic circulation The arterial blood therefore contains increased quantities of reduced hemoglobin producing visible cyanosis

An important factor contributing to the development of cyanosis is the reduction in pulmonary blood flow Since systemic venous blood is shunted away from the pulmonary circuit into the aorta pulmonary blood flow is less than systemic flow Mechanisms increasing pulmonary flow are beneficial under these conditions For example children may not have visible cyanosis for months or years after birth closure of the ductus arteriosus is frequently delayed However as the ductus arteriosus finally closes the degree of cyanosis and severity of the patient's clinical condition usually become worse Thus the equalizing effect of a patent ductus arteriosus on pulmonary and systemic flow is beneficial *even though the* arterial blood passing into the pulmonary artery is only slightly unsaturated and can take up only limited quantities of oxygen during passage through the lungs This is the functional basis for one approach to therapy of tetralogy of Fallot and related lesions (see Fig 16) Many patients improve to varying degrees between 5 and 9 years of age presumably because bronchial flow through the alveolar membranes increases by a mechanism similar to that operative when pulmonary flow is obstructed by an embolus (see Fig 3*B* Chapter 4) The dilated bronchial arteries serve to supplement pulmonary blood flow just like a patent ductus arteriosus or an artificial shunt (see Fig 16)

CLINICAL SIGNS OF TETRALOGY OF FALLOT The typical roentgenographic changes in patients with tetralogy of Fallot include diminished pulmonary vascular markings in the peripheral lung fields on teleroentgenograms and during fluoroscopy The shadows in the hilar region may be prominent but are disorganized apparently because the bronchial arteries are dilated (Fig 15*C*) Infundibular stenosis is generally associated with a small pulmonary artery which leaves a prominent convexity in the mid portion of the left border of the cardiac silhouette Right ventricular hypertrophy tends to elevate the apex of the heart The resulting cardiac silhouette is shaped like a wooden shoe the *cor en sabot* However right ventricular hypertrophy is more easily demonstrated with the patient in the left anterior oblique position The enlarged right ventricle protrudes anteriorly toward the sternum and increases the angulation at the junction of the right ventricle and the ascending aorta The space enclosed within the aortic arch—the aortic window—is abnormally clear if the pulmonary artery and its main branches are smaller than normal A small proportion of patients with tetralogy of Fallot have pulmonary valvular stenosis instead of infundibular stenosis In this disorder the peripheral lung fields are clearer than normal but the pulmonary arterial trunk is distended by the post-stenotic dilatation which appears as a prominent bulge on the left border of the cardiac silhouette viewed in the postero-anterior *position (Fig 15E)*

Right ventricular hypertrophy produces the characteristic changes in the electrocardiographic pattern but this may be somewhat obscured by the ventricular conduction disturbance which commonly accompanies defects in the ventricular septum The P waves are generally tall and peaked in leads I and II indicating right atrial enlargement Loud coarse systolic murmurs are widely transmitted over the precordium, but have maximum intensity in the third left intercostal space Unfortunately, these murmurs are not sufficiently distinctive to permit tetralogy of Fallot to be distinguished from other congenital or acquired lesions on the basis of auscultatory findings A definitive diagnosis can be made by cardiac catheterization in which a catheter is passed

SURGICAL THERAPY OF INSUFFICIENT PULMONARY FLOW

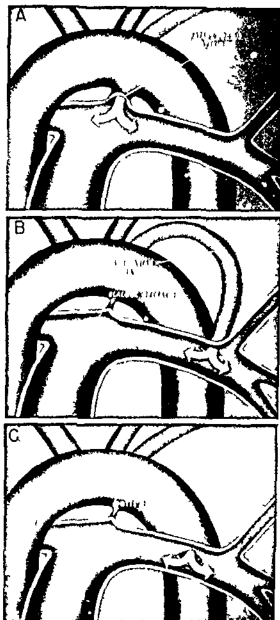


FIGURE 16 *A* In patients with tetralogy of Fallot or other congenital deformities including obstruction of flow into the pulmonary artery the *pulmonary* blood flow *is supplemented* by blood flowing through a patent ductus arteriosus When the ductus arteriosus closes spontaneously total pulmonary blood flow is diminished cyanosis becomes worse and exercise tolerance is further reduced

B By joining a subclavian artery to a branch of the pulmonary artery Blalock produced an artificial ductus arteriosus to supplement pulmonary blood flow

C A direct anastomosis of the aorta to the pulmonary artery was developed by Potts as an alternative *method for* producing an artificial ductus arteriosus

These surgical procedures often produce dramatic improvement in the condition of patients with scanty pulmonary blood flow even though systemic arterial blood is used to supplement pulmonary flow

through the interventricular septal defect into the aorta Pulmonary stenosis is indicated by a marked pressure drop between *the right* ventricle and the pulmonary artery (see Fig 11, Chapter 18)

TREATMENT OF TETRALOGY OF FALLOT The beneficial effects of a patent ductus arteriosus on patients with tetralogy of Fallot led to the development of the Blalock-Taussig operation Anastomosing a subclavian artery to a pulmonary artery produces an artificial ductus arteriosus and increased pulmonary blood flow (Fig 16*B*) The Pott's modification of this procedure involves a direct anastomosis between the pulmonary artery and descending aorta (Fig 16*C*) Definite improvement followed these procedures because pulmonary blood flow was supplemented even though the artificial shunts carried partially oxygenated blood from the systemic system In other words, pulmonary flow more nearly approaches systemic flow if these procedures are successful From a functional point of view, it is far more important to remove the obstruction to the flow of systemic venous blood from the right ventricle into the pulmonary artery A direct attack on the pulmonary stenosis with infundibular resection or valvulotomy (see Fig 12, Chapter 18) *is more* physiologic than an artificial shunt However, this approach has proved particularly valuable in patients with valvular stenosis while infundibular resection is a much more dangerous procedure

Tricuspid Atresia

If the tricuspid orifice is blocked during embryologic development, the right ventricle fails to develop normally and persists as a small rudimentary chamber Since venous blood from the systemic circuit cannot enter the right ventricle directly, it must flow through a defect in the interatrial *septum (Fig 17A) In the left* atrium this unsaturated blood mixes with the oxygenated blood returning from the lungs The mixed blood then enters a large left ventricular cavity Blood ejected from this functionally

single ventricle flows readily into the aorta but must pass through an interventricular septal defect into the rudimentary right ventricle and then into the pulmonary artery (Fig 17*B*) As if this were not enough most of these patients have pulmonary stenosis either in the form of a long narrow infundibular channel or a valvular diaphragm with a small central perforation The high resistance to flow past these obstructions restricts pulmonary blood flow and results in cyanosis as indicated in Figure 13*C*

The severity of the cyanosis and diminished exercise tolerance is related to the degree of resistance to flow into the pulmonary artery Most patients have severe pulmonary stenosis and correspondingly severe

TRICUSPID ATRESIA

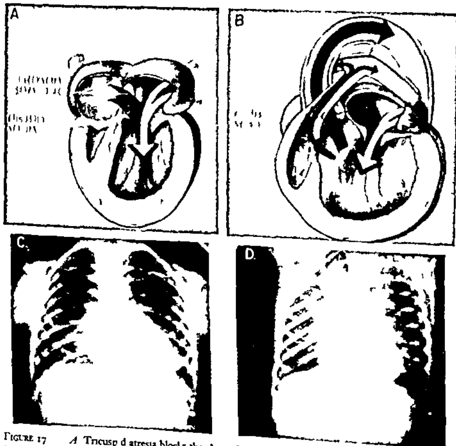


FIGURE 17 *A* Tricusp d atresia blocks the channel between the right atrium and right ventricle so the entire systemic venous return must pass through an atrial septal defect and mix with pulmonary venous blood in the left atrium

B The mixed blood enters the left ventricle Blood ejected from this single chamber flows readily into the aorta but must pass through an interventricular septal defect into a rudimentary right ventricular chamber Flow into the pulmonary artery is usually restricted by either infundibular or pulmonary valvular stenosis so pulmonary blood flow is less than systemic flow This cond tion often leads to severe cyanosis as indicated in Figure 13 However if the channel to the lungs offers sl ght resistance and pulmonary flow exceeds systemic flow cyanosis can be sl ght

C In the frontal view the cardiac silhouette has a concave left border similar to tetralogy of Tallot (Fig 15) The p lmonary vascular markings are usually diminished and disorganized

D In the left anterior oblique view the anterior margin is flattened because of the diminutive right ventricle In some patients presystolic pulsation of the right atrium can be observed on the anterior border of the heart because this chamber is not hidden behind the right ventricle The left ventricle projects posteriorly over the spine and left ventricular preponderance is demonstrated electrocardiographically

cyanosis However, I have seen a 17 year old girl with this lesion who had moderate cyanosis and *prominent clubbing of the* fingers, and yet was quite athletic, indulging in sports such as swimming The pulmonary vascular markings indicated unusually good pulmonary blood flow Theoretically, if the pulmonary resistance is slight and pulmonary blood flow is greater than systemic flow, arterial unsaturation need not be sufficient to produce visible cyanosis although the blood from the lungs and systemic veins is mixed in the single ventricle (see Fig 13)

Diagnosis of Tricuspid Atresia Because of the small pulmonary outflow tract and pulmonary artery, the left border of the heart is concave, closely resembling tetralogy of Fallot in the frontal projection The pulmonary vascular markings are diminished in the peripheral lung fields, and the hilar shadows generally appear disorganized from dilatation of the bronchial vessels (Fig 17*C*) Viewed in the left anterior oblique position, the cardiac silhouette is usually flattened anteriorly (*Fig 17D*) Owing to the hypoplastic condition of the right ventricle, the right atrium may be prominent on the sternal border and presystolic movement of this portion of the silhouette constitutes a fluoroscopic sign of tricuspid atresia Evidence of left ventricular enlargement appears on both roentgenograms and electrocardiograms Thus, cyanosis associated with diminished pulmonary blood flow and left ventricular enlargement are the characteristic features of this condition

Treatment of Tricuspid Atresia Pulmonary blood flow can be augmented by an artificial ductus produced by either the Blalock-Taussig operation or the Pott's modification (Fig 16)

Truncus Arteriosus

A persistent truncus arteriosus with a

TRUNCUS ARTERIOSUS

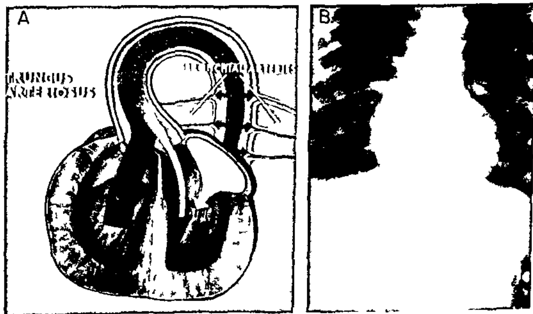
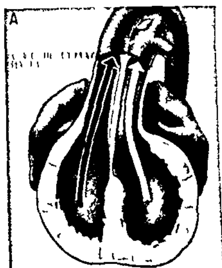


Figure 18 *A* If the pulmonary arteries fail to develop the truncus arteriosus persists and the lungs are served solely by dilated bronchial arteries (see Fig 3 Chapter 4) The blood flow through the lungs is scanty so the oxygenated blood is mixed with larger volumes of highly unsaturated systemic venous blood and cyanosis is very intense Most patients with this condition usually succumb during the first few weeks of life

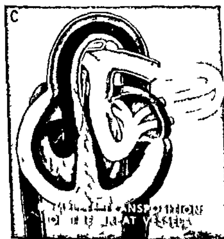
B On roentgenograms exposed in the postero-anterior position the left border of the cardiac silhouette is concave and the mediastinum is very narrow because the pulmonary artery is missing The lung fields are abnormally clear and the pulmonary vascular shadows are spotty and lack continuity In the left anterior oblique view the heart shadow resembles an apple suspended from a curved stem as suggested by the contours of the schematic drawing in *A* The right ventricle forms an angle of almost 90 degrees with the ascending aorta a condition known as shelving

large pulmonary artery branching off was considered in the section on large shunts with pulmonary hypertension and acquired cyanosis If the truncus arteriosus persists because the pulmonary artery is absent the lungs are served only by dilated bronchial arteries (Fig 18A) Under these conditions pulmonary blood flow is extremely sparse

COMPLETE TRANSPOSITION OF THE ARTERIAL TRUNKS







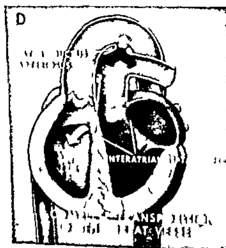


FIGURE 19 *A* The spiral form of the aortic pulmonary septum accounts for the manner in which the aorta and the pulmonary arteries are entwined in the fully developed heart (see Fig 3) If the aortic pulmonary septum were straight, the arterial trunks would be parallel and the right ventricle would empty into the aorta and the pulmonary artery would arise from the left ventricle

B A specimen from a patient with complete transposition of the great vessels demonstrates the parallel courses of the aorta and pulmonary artery suggested in *A* Furthermore, the arterial trunks arise from the wrong ventricles

C When the arterial trunks are completely transposed systemic venous blood enters the right ventricle and is pumped directly back into the aorta Oxygenated blood from the pulmonary veins enters the left ventricle and is recirculated right back through the lungs All the partitions of the heart serve to obstruct the flow of systemic venous blood to the lungs

D Complete transposition of the great vessels would be fatal immediately after birth unless there are communications between these two independent circulatory systems Through defects in the atrial or ventricular septa or through a patent ductus arteriosus sufficient exchange of blood may occur to support life In this case larger defects in the partitions of the heart are most advantageous and on occasion have been induced surgically

and cyanosis is severe immediately after birth Most patients with this type of lesion expire during the first few weeks of life No surgical therapy for the condition has been devised Since the pulmonary artery is missing, the cardiac silhouette has a concave left border in the frontal view (Fig 18*B*) The ventricular shadow often appears rounded and the mediastinal shadow is often narrow In the left anterior oblique position, the heart shadow is reminiscent of a large apple suspended on a stem, the truncus arteriosus (Fig 18*A*)

Complete Transposition of the Arterial Trunks

If the truncus arteriosus is divided by a straight septum rather than the normal spiral septum the right ventricle pumps systemic venous blood into the aorta and the left ventricle ejects oxygenated blood back through the pulmonary artery (Fig 19*A*, *C*) When the arterial trunks are transposed in this manner (Fig 19*B*), all the normal partitions dividing the heart act to obstruct the flow of systemic venous blood into the lungs If no defects in the partitions remain none of the oxygenated blood from the lungs can be distributed to the tissues of the body and the patient promptly expires (Fig 19*C*) On the other hand, *any patient with a large* atrial septal defect and a large patent ductus arteriosus has a chance of surviving at least *for some years (Fig 19D)* If only one shunt persists between the pulmonary and systemic circuits, flow through the shunt must periodically reverse its direction This means that the pressures on the two sides of the communication must fluctuate in opposite directions One such patient survived for 11 months with extremely severe cyanosis from birth Her venous blood was extremely viscous and nearly as black as tar Postmortem examination disclosed that the only communications between the systemic and pulmonary systems consisted of three small interatrial septal defects, none of which was larger than a match head The ductus arteriosus was obliterated That patients can survive with such low oxygen tensions in the blood and tissues seems incredible

The pressures in the systemic and pulmonary circuits are approximately equal when flow is periodically reversed through shunts between them Under these con-

ROENTGENOGRAMS IN COMPLETE TRANSPOSITION



FIGURE 20 *A Complete transposition of the great vessels is the only condition producing severe cyanosis* from birth in the presence of pulmonary congestion Since the pulmonary artery lies behind the ascending aorta, the mediastinal shadow is narrow in the frontal view and the left border of the heart is concave This roentgenogram was taken on a patient at 4 months of age

B At the age of 28 *months the* cardiac silhouette was greatly enlarged This is a characteristic feature of complete transposition of the great vessels and frequently obscures the narrow mediastinal shadow

C By 34 months the heart had become tremendous virtually filling the thoracic cavity

ditions pulmonary vascular pressures are greatly elevated and the lungs are congested For this reason, the pulmonary vascular markings are accentuated and pulsate vigorously This is the only congenital malformation with severe cyanosis from birth with evidence of increased pulmonary blood flow In most patients the size of the cardiac silhouette increases progressively to reach a massive degree of enlargement in the first few months of life (Fig 20) This cardiac enlargement has been ascribed to a deficient oxygen supply to the myocardium Such an explanation may be particularly *applicable to those* patients in whom the coronary arteries arise from the aorta and are perfused with systemic venous blood with its very low oxygen tension Currently *the only* treatment consists of producing or expanding shunts between the systemic and pulmonary circuits An artificial ductus arteriosus (Fig 16) or a surgically induced *interatrial* septal defect augments the exchange between the two independent systems With the development of the mechanical heart lung apparatus to take over cardiopulmonary function during surgery it may be possible to correct this condition by reversing the origins of the arterial trunks This technique also has important potential applications in direct surgical *correction of* many of the congenital malformations of the heart

SUMMARY

The embryologic development of the heart is so complex that one may marvel that congenital malformations are not common. Most of the developmental defects are *due* to incomplete development of partitions which divide a single convoluted tube *into* four chambers and corresponding arterial trunks Since the pulmonary resistance normally becomes much less than systemic resistance after delivery into *the external* world the pressures in the left atrium *left* ventricle and aorta are much higher than those in the corresponding channels carrying systemic venous blood to the lungs For this reason, oxygenated blood returning from the lungs is diverted through the shunts into the right chambers or pulmonary artery to be recirculated back through the lungs Therefore all the simple shunts have common features representing compensation to increased pulmonary flow

Large shunts between the left and right ventricles and between the aorta and pulmonary artery theoretically could divert virtually all the output of both ventricles through the lungs leaving insufficient flow through the systemic arteries to support life This contingency is prevented by a greatly increased pulmonary resistance which approaches or even exceeds systemic resistance Under these *conditions the* systemic and pulmonary blood flows are roughly balanced Excessive *pulmonary* resistance sometimes develops which *diverts* unsaturated blood returning from the systemic veins into the systemic *arteries to* produce acquired cyanosis Certain common *congenital malformations* characteristically cause cyanosis because anatomic *arrangements impede* or restrict the flow of systemic venous *blood into the lungs* In each type *of lesion it is* important to consider the location *of* the septal defects and the site and nature of the obstruction to flow of unsaturated systemic blood into or *through the* pulmonary circuit

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rheumatic mitral valvular disease with cardiac decompensation However if some of the key points in the pattern are missing a more conservative attitude toward the diagnosis is required

The main symptoms associated with heart disease include dyspnea and orthopnea reduced exercise tolerance or fatigue precordial pain and cyanosis The principal signs which are elicited during routine examination include evidence of enlargement of cardiac chambers (e g, on roentgenograms and electrocardiograms) alterations in the rate and rhythm of the heart beat changes in the conduction system and in the physiologic state of the myocardium as assessed from altered electrical activity, alterations in heart sounds and the presence of murmurs and changes in venous and arterial pressure Certain confirmatory signs are valuable even though they are not directly referable to the heart (chorea subcutaneous nodules substitution symptoms with coronary occlusion clubbing of the fingers etc)

If one considers the limited sources of information the accuracy of cardiac diagnosis which has been achieved is truly remarkable However recognizable patterns generally occur only in advanced stages of disease processes In the early stages when diagnosis is even more important to the welfare of the patient the combination of diagnostic clues is often either incomplete or atypical In many instances a patient may exhibit only a single stigma A diagnosis can rarely be made from an isolated clue since a single sign cannot establish a pattern Even if several signs are present it is necessary to ascertain that each is beyond the range of normal a decision that is not always easy because of biologic variability

BIOLOGIC VARIABILITY

No two living organisms are the same even though they belong to the same species For this reason a particular characteristic cannot be precisely described in such a way that it includes all individuals This fact becomes apparent when one attempts to determine such a simple trait as the normal body temperature In spite of the little red arrow pointing to 98 6 F on a clinical thermometer the oral temperatures among normal individuals are spread over a considerable range The degree of variability in oral temperature can best be described as a curve of frequency distribution determined by recording the temperatures of a large number of healthy subjects and plotting the incidence of each recorded value (Fig 1) If

THE RANGE OF NORMAL

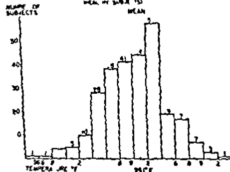




FIGURE 1 *A* In a large group of subjects the normal oral temperatures recorded under controlled conditions are spread over a considerable range with the largest number of values falling near the mean for the group A frequency distribution of this general type can be derived from a sufficiently large series of virtually any physiologic or anatomic measurement (e g erythrocyte count pulse rate intensity of heart sounds basal metabolic rate height) Such biologic variability complicates a description of normal and confuses the question of abnormality

B If a particular variable is altered by some disease process a frequency distribution of measurements on a selected group of patients may differ from that of normal subjects Each clinical sign or laboratory test must be evaluated in terms of the likelihood that it is a variant of normal (i e., within the normal range) or is an evidence of abnormality This distinction is very difficult in "borderline patients who may appropriately receive a diagnosis of possible disease if inadequate confirmatory evidence is available

Chapter 20

Possible Heart Disease

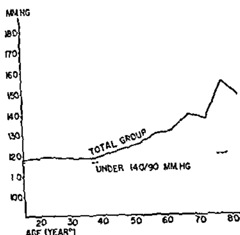
The ultimate goal in cardiac diagnosis is to establish the nature of the anatomic and functional disorder and to assess its severity The preceding chapters indicate an approach to the diagnosis of various common types of heart disease It is not always possible to arrive at a definite diagnosis from the information which can be obtained with available techniques In fact, there is a fairly large group of persons in whom it is impossible to be certain whether the heart is *normal or abnormal To them, the diagnosis* of *possible heart disease* is quite properly applied, because placing a label of heart disease on a healthy person can have serious psychologic, social and financial implications, affecting not only the individual but his whole family Persons whose disorders fall into the category of possible heart disease are not necessarily informed of the suspicions the physician may have However, this diagnosis has implications which cannot be brushed aside, namely, the necessity for extending the period of observation until there is adequate evidence to substantiate a definite conclusion Even though the incidence of possible heart disease may be higher than that of any other single category *of heart ailments the question is rarely* raised in textbooks of cardiac diagnosis This chapter is devoted to a consideration of problems *presented by patients for whom* a definite diagnosis cannot be assigned

THE IMPORTANCE OF DIAGNOSTIC PATTERNS

The number of different heart diseases greatly exceeds the number of diagnostic signs and symptoms This fact means that the same signs and symptoms accompany different types of heart disease, and that a specific diagnosis depends upon recognizing a characteristic pattern of signs and symptoms occurring in a particular temporal sequence When a patient displays the full set of typical signs and symptoms appearing in a reasonable sequence, a specific diagnosis can be confidently made

The preceding chapters in Part V contained *descriptions of some common* patterns encountered in patients with various types of heart disease One example of such *a pattern would be a definite history of re*current attacks of acute rheumatic fever (as illustrated by the pattern shown in Fig 3, Chapter 17), combined with the symptoms of dyspnea on exertion and reduced exercise tolerance for years (Fig 4, Chapter 9) Superficial examination reveals abundant peripheral congestion and edema (see Fig 5 Chapter 9) The heart is enlarged to percussion and a diffuse precordial impulse is noted over the precordium to the left of the sternum (Figs 2 and 3, Chapter 11) Roentgenography demonstrates enlargement of the left atrium, right ventricle and right atrium (Figs 12 and 13, Chapter 11) The pulmonary vascular markings are increased Electrocardiography confirms the right ventricular *preponderance* (Fig 22 Chapter 15), and the P waves in leads I and II are prolonged flattened and notched indicating *left atrial enlargement* (Fig 23*B* Chapter 15) During careful auscultation near the apex of the heart, a presystolic *murmur, a diastolic rumble and a systolic* murmur are noted (Fig 9 Chapter 18) The second sound in the pulmonary area is very loud and ringing *A physician confronted* by a patient with such a complete pattern of diagnostic signs would have considerable confidence in a diagnosis *of advanced*

CRITERIA FOR NORMALITY



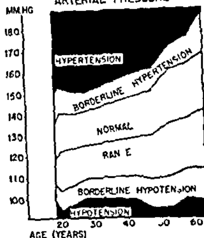


FIGURE 2 Although systemic arterial hypertension is often regarded as a diagnosis elevated arterial pressure is really a sign of peripheral vascular abnormality The principal difficulty lies in defining the levels of blood pressure which are beyond the range of normal. It is generally recognized that arterial blood pressure rises progressively with age which must be taken into account in defining normality in a group of patients.

A The increase in systolic arterial pressure with advancing age in a large group of individuals is indicated by the solid line When systolic pressure readings of patients who ultimately attained systolic pressure above 140 mm. Hg were eliminated the remainder of the group evidenced little elevation in blood pressure over many years This observation led Robinson and Brucer[3] to conclude that the arterial blood pressure does not increase significantly with age in most individuals and that any value persistently above some level (such as 120 80 mm. Hg) indicates either hypertension or incipient hypertension.

B In contrast broad ranges of normal systolic pressures were established from a similarly large group of subjects by Master et al.[5] In addition, borderline ranges of both hypertension and hypotension were described If these criteria are used, systolic pressure values falling between 110 and 160 are included in the normal range and the borderline ranges extended the values to include the range between 100 and 180 mm Hg in the older age groups These two examples illustrate how divergent criteria for normality may be derived from similar sets of data.

applied Therefore high blood pressure is not truly an exception to the principle that a diagnosis cannot be made with confidence on the basis of a single isolated sign

Isolated Murmurs

Many patients with patent ductus arteriosus have only a characteristic murmur with no subjective symptoms and no other *objective evidence of disease* The continuous murmur is *sufficiently distinctive* that a physician can create a *most favorable* impression by confidently *diagnosing* a patent ductus arteriosus on the basis of auscultation alone However he runs the risk of being tripped up by the exceptional patient with an aortic septal defect (see Fig 11 Chapter 19) Similarly the opening snap of mitral stenosis is widely regarded as a pathognomonic sign However if a brief high pitched sound in early diastole were heard not accompanied by murmurs in a patient with no other evidence or history of disease it would be folly to recommend commissurotomy on the basis of such meager data A more logical *approach* would be to assign the diagnosis of possible heart disease and continue observations until a more definite diagnosis could be established A much more common source of difficulty along this line results from the widespread occurrence of systolic murmurs in both normal persons and patients with heart disease

Systolic Murmurs

Turbulence due to the rush of blood through pulmonary artery and ascending

the number of subjects is large enough, a roughly bell-shaped curve is the result which indicates the normal range of this variable In a study by Ivy,[1] the oral temperature in a group of healthy subjects averaged 98 1, but varied between 96 5 and 99 3 Furthermore, the body temperature varies more than 1° F during the day For this reason, a single reading for body temperature should be at least 2 4° F away from the mean value to be considered abnormal [2] However, if a group of patients with febrile illnesses is tested, the oral temperatures describe another frequency distribution with the mean at a higher level than that for the normal group Some of these patients will have oral temperatures within the normal range In other words, the two curves overlap (Fig 1*B*)

Curves for virtually all signs and symptoms exhibit overlap between groups of normal subjects and of diseased patients For example, the heart rate among healthy subjects can vary from 50 to 100 beats per minute, and patients with infectious diseases or complete atrioventricular block have pulse rates within this range Similarly, patients with either patent ductus arteriosus or aortic insufficiency may have normal systemic arterial blood pressures For such reasons as these, determining the normality of a particular sign of disease is frequently difficult A broad range of normality limits diagnostic reliability and usefulness of signs

Systemic Arterial Hypertension

A sustained elevation of systemic arterial blood pressure imposes a pressure load on the left ventricle It is frequently considered among the forms of heart disease By definition, the diagnosis of hypertension depends solely upon establishing that the systemic arterial pressure is abnormally high Opinions vary concerning the normal range of both systolic and diastolic pressures For example, Robinson and Brucer[3] reported a statistical study of arterial pressure values of 11,883 persons and serial records from 500 persons observed for 5 to 10 years They concluded that the normal range of systolic blood pressure for men and women is from 90 to 120 mm Hg and the range of diastolic pressure extends between 60-80 mm Hg They eliminated individuals with "obvious hypertension" and stated that the blood pressure in the remainder of the subjects remained fairly constant over a period of years (Fig 2*A*) For this reason, they concluded that arterial blood pressures remaining above 120 systolic and 80 diastolic over a 10 year span in either men or women are pathologic and are an almost infallible sign of incipient hypertension Thus, they considered slightly more than 40 per cent of the adult population "actually or incipiently" hypertensive Treloar[4] criticized the statistical methods employed in this study, pointing out, among other things, that rejecting individuals with pressure levels above an arbitrary level biases the results in favor of a predetermined conclusion Master et al [5] analyzed data from 15,706 men and women ranging in age from 16 to 65 years and established much more liberal ranges of normal values for systolic pressure (Fig 2) Even with the broad range of normality illustrated in Figure 2, Master and his co-workers included a borderline range for "possible hypertension" and "possible hypotension" These borderline ranges correspond to the overlap between normal subjects and patients with febrile illnesses in Figure 1 Although this more liberal view of normality is more acceptable to most physicians, it indicates the limited usefulness of the measurement Since the blood pressure in a healthy subject may rise to abnormal levels simply as a result of a visit to a physician's office considerable care must be exercised to avoid applying the label 'hypertension' to normal persons

Although arterial hypertension is commonly treated as a diagnosis, it is actually only one manifestation of a number of pathologic processes Unfortunately, the etiology of the high blood pressure is unknown in the large group of individuals to whom the term *essential* hypertension is

velographs[8] Comparisons were made of the information gained from auscultation by three physicians from sonvelograms and from standard phonocardiograms recorded with a Sanborn Stethocardiette The physicians reported their impressions by drawing sketches indicating the intensity of the sounds and murmurs they heard over at least four positions on the precordium (Fig 3) In form these sketches resembled the sonvelographic patterns but were supplemented by notations concerning the frequency or quality of the sounds or murmurs When these sketches and machine records were obtained on unknown patients with various types of well-established heart disease they agreed very well However in a study of 211 unselected school children ranging in age from 7 to 10 years the extent of disagreement among the five sources of information was appalling For example the most common notation on all records was an early systolic murmur In only 44 subjects did all sources of information agree concerning the presence of such murmurs three agreed in an additional 40 subjects In 30 more subjects early systolic murmurs were noted on just two records

Eighteen subjects were brought to the University for further study because one or more of the examinations were reported as either possible heart disease or organic heart disease On this occasion six examiners participated in the auscultatory examination which was supplemented by clinical history both types of phonocardiography fluoroscopy sedimentation rates antistreptolysin titers and the Wetzel grid Even after careful evaluation of each patient unanimous agreement among the group of examiners was rare For purposes of tabulation a majority vote was taken Six patients were classed as definite organic heart disease nine were still in the category of possible heart disease and three were considered to have functional murmurs It was impressive to note that the records of all six participants agreed unanimously on only 4 of the 18 patients of which two were later believed to have organic heart disease and the other two had murmurs classed as functional Another point of interest was the demonstration that certain of the examiners consistently missed low frequency vibrations such as third heart sounds or certain diastolic murmurs The principal lesson gained from this study was the fact that a patient with suspicious murmurs and no other evidence of heart disease is quite properly classed as possible heart disease Periodic examinations over long intervals may be required before a reasonable conclusion can be reached To do this without producing unnecessary psychologic trauma on the patient and the family is difficult but extremely important

Diastolic murmurs are much more reliable evidence of organic disease of heart valves than are systolic murmurs However the diastolic murmurs which occur during initial attacks of acute myocarditis do not necessarily indicate that the mitral valve is functionally stenotic (see Figs 5 6 12, 13, *Chapter 17*)

Electrocardiographic Signs

Electrocardiography has proved so valuable in providing supplemental information for cardiac diagnosis that its limitations are too frequently disregarded Extensive alteration in electrocardiographic patterns can occur without any other evidence of cardiac disease a fact which should not be forgotten or ignored

Prolongation of the P R interval may result from increased discharge of the parasympathetic fibers distributed to the atrioventricular node Indeed this mechanism has been postulated to explain the increased atrioventricular nodal delay in patients with acute rheumatic fever Silverman and Goodman[9] described a patient with neurocirculatory asthenia in whom the P R interval became prolonged without obvious cause to 0 72 second more than three times the upper limit of normal Wolfram[10] found that among 52 patients with severe ventricular conduction disturbances 33 had no

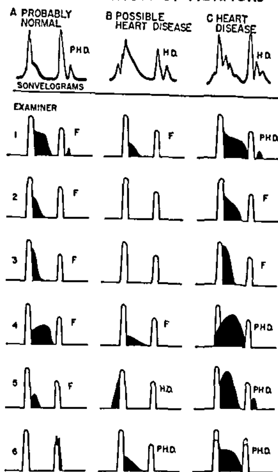


FIGURE 3 Differences in the perception and interpretation of sounds and murmurs are illustrated by three examples selected from a study of 211 unselected school children At the top of each column is a sonvelographic pattern and below are reproductions of the sketches drawn by six examiners to represent the intensity and timing of sounds and murmurs The individual interpretations are indicated as follows F Functional P H D Possible Heart Disease H D, Heart Disease

A An early systolic murmur was noted on the sonvelograms and by five of the six examiners A third heart sound was noted by one examiner and on the two types of heart sound records This patient was later classed as probably normal because of the nature of the murmur and because no other evidence of heart disease could be elicited

B In another child no murmurs were noted by two examiners an early systolic murmur was indicated on three of the sketches and one examiner described a presystolic murmur which he felt meant that organic heart disease was present Evidence of diastolic murmurs was noted on sonvelograms and phonocardiograms The patient had a history suggestive of previous rheumatic fever Slight left ventricular enlargement was reported after fluoroscopy and the patient s condition was classed as possible heart disease because the evidence was equivocal and incomplete

C, Prominent systolic murmurs were noted by all examiners and an early diastolic sound was heard by two Phonocardiograms indicated an early systolic murmur and diastolic vibrations in both the early diastolic and presystolic intervals Fluoroscopy indicated right ventricular enlargement Later the patient was found to have been under the care of a physician because of previous attacks of acute rheumatic fever

These examples indicate the difficulties in arriving at a decision concerning the nature and significance of heart murmurs during early stages of heart disease when the signs have not fully developed

aorta is a normal phenomenon (see Fig 16, Chapter 13) Thus, the basis for an early systolic murmur occurs in virtually all members of the population However, these vibrations may not be audible if they are not sufficiently intense to reach the auditory threshold of the examiner In other words, the auditory mechanism itself, also subject to biologic variations, imposes an arbitrary limit which determines whether a murmur is present or absent so far as an observer is concerned Phonocardiographs can record vibrations below the auditory threshold, but to date we lack criteria for evaluating the significance of inaudible murmurs

Attempts to describe the distinguishing features of "functional" systolic murmurs are rather vague at best For example Evans[6] indicated that it takes considerable experience to judge the intensity of functional murmurs, but that "it is enough to remember that it is neither a loud nor a long murmur There is one notable exception to the rule—namely, that when the murmur is *late* in systole and placed as near to the second heart sound as the first it can be loud (and usually it is loud) and yet it is an innocent murmur " I remain unconvinced that a late systolic murmur at the apex is categorically innocent Most clinicians have their own individual criteria for recognizing functional murmurs Unfortunately, these criteria vary widely among physicians This point was discussed by Stewart [7] who called attention to the difficulty in obtaining corroboration of any judgment concerning a systolic murmur The problem posed by isolated systolic murmurs in children was forcefully emphasized for me during a study designed to evaluate the usefulness of son-

disease must be applied at times to patients with any type of heart disease should be a constant reminder that much remains to be accomplished in improving and refining our diagnostic methods

SUMMARY

The general principles which have been brought out by considering only a few common evidences of heart disease actually apply to virtually all the diagnostic signs used in clinical medicine A specific diagnosis of abnormal cardiac structure and function is almost invariably based on patterns of clinical history symptoms signs and laboratory tests If the pattern is incomplete or atypical disease of the heart may be definitely indicated but its nature may remain obscure Each item in the pattern must be considered to determine if it is beyond the range of normal for the individual patient A single evidence of abnormality is rarely sufficient to establish a diagnosis Indeed it is often difficult to establish the presence of heart disease without more than one diagnostic sign.

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ISOLATED ELECTROCARDIOGRAPHIC SIGNS

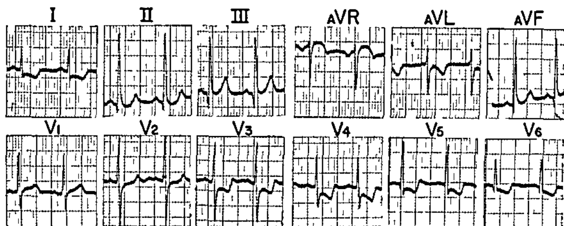


FIGURE 4 If this electrocardiogram had been obtained from a 50 year old executive with a history of angina pectoris and severe precordial pain a diagnosis of acute myocardial infarction might be entertained However this record was obtained from a boy aged 9 years who was first seen five years before because of left hydronephrosis later treated by nephrostomy and finally by nephrectomy Prior to operation a blowing systolic murmur was noted in the mitral area and the pulmonary vascular markings were reported to be accentuated The electrocardiographic patterns were within normal limits He was followed in the cardiac clinic Three years later he had no audible murmurs and no definite evidence of heart disease On 6/3/53 his mother stated that he was better than he had ever been his exercise tolerance and growth had improved and he had neither symptoms nor evidence of any illness On that visit electrocardiographic patterns very similar to those seen *above were noted for the first time The abnormalities of the S T segment and T waves have persisted until* the present time with no complaints and no evidence of heart disease The extreme alterations in the electrocardiogram unaccompanied by other confirmatory evidence are not sufficient for a diagnosis However, the patient has been classed as *definite* heart disease *probable* heart disease *possible* heart disease and normal by different physicians who have seen him This is an example of the diagnostic problems which may result from an isolated sign of disease

clinically evident cardiac disease (see also Fig 26, Chapter 15) Some patients with traits of anxiety display deviation of the S-T segment and alterations in the T waves in various leads which may be reversed by reassurance and retesting at a later date [11]

The configuration of electrocardiographic complexes can be altered by many everyday activities including *changing the position of* the body or eating an ordinary meal [12] The number of factors which can induce changes in electrocardiographic patterns is extremely large and all too frequently overlooked For example, Lepeschkin[13] devoted four chapters to a review of the physiologic, physical, chemical, and hormonal factors which can alter the form of the various complexes Before the label "heart disease is applied to a patient on the basis of electrocardiographic patterns alone, the various extraneous factors should be excluded as far as practicable

The circumstances in which an *electro-*cardiographic change develops are extremely important in its interpretation For example, a physician presented with the electrocardiogram in Figure 4 and no other information about the patient might possibly suspect an acute myocardial infarction However, these records were actually obtained from a 9 year old boy during a period when he had *neither signs nor symptoms referable to his* heart Since the changes in configuration of the complexes are far beyond the limits of normal" for this age he may have heart disease, but its nature is completely indeterminate unless or until other evidence becomes manifest

The clinical implications of isolated signs and symptoms could be discussed exhaustively, but such an essay would require reviewing the entire subject of cardiac diagnosis in the light of this new emphasis Actually, this problem has been considered in many sections of the preceding chapters *The fact that the diagnosis of possible heart*

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